INVENTOR SEARCH

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FILE COVERS 1907 - 2 Aug 2007  VOL 147 ISS 6
FILE LAST UPDATED: 1 Aug 2007  (20070801/ED)

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 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d que nos l21
L1              STR
L3             50 SEA FILE=REGISTRY SSS FUL L1
L5              STR
L7              7 SEA FILE=REGISTRY SUB=L3 SSS FUL L5
L8             26 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3
L9              3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7
L10        133107 SEA FILE=HCAPLUS ABB=ON  PLU=ON  C11/OBI OR 11C/OBI OR
                  CARBON/OBI(1A)11/OBI OR 18F/OBI OR F18/OBI OR FLUORINE/OB
                  I(1A)18/OBI OR RADIOLABEL?/OBI OR LABEL?/OBI OR ISTOPE/OB
                  I OR RADIOPHARMA?/OBI OR RADIO/OBI(W)PHARM?/OBI OR
                  IMAG?/OBI (W) (COMPD/OBI OR COMPOUNDS/OBI OR COMPN/OBI)
L11             4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 AND L10
L12             4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 OR L11
L16           487 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BRADY, F?/AU
L17           110 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LUTHRA S?/AU
L18            49 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND L17
L19            13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L18 AND IMAGING/OBI
L21            22 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 NOT (L12 OR L19)


=> d ibib ed abs l21 1-22

L21  ANSWER 1 OF 22  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        2007:679886  HCAPLUS  Full-text
TITLE:                   In vitro and in vivo characterization of
                         [3H]CNS-5161, a use-dependent ligand for the
                         N-methyl-D-aspartate receptor in rat brain
AUTHOR(S):               Biegon, Anat; Gibbs, Andrew; Alvarado, Maritza;
                         Ono, Michele; Taylor, Scott
CORPORATE SOURCE:        Medical Department, Brookhaven National
                         Laboratory, Upton, NY, USA
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SOURCE: Synapse (Hoboken, NJ, United States) (2007), 61(8), 577-586
CODEN: SYNAET; ISSN: 0887-4476
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 24 Jun 2007
AB Glutamate is the major excitatory neurotransmitter in the brain. Glutamate activation of the N-methyl-D-aspartate (NMDA) receptor subtype is thought to mediate important physiol. and pathol. processes, including memory formation and excitotoxicity. The goal of the present work was to characterize and validate a candidate agent for noninvasive positron emission tomog. (PET) imaging of this receptor. [3H]-labeled N-[3-3H]-methyl-3-(thiomethylphenyl)cyanamide (CNS-5161) was incubated with rat brain homogenates at increasing concns., temps., and times to establish the binding kinetics and affinity of the ligand in vitro. Nonspecific binding was measured with 100 μM MK-801. The compound was also injected i.v. in rats pretreated with saline, NMDA, MK801, or a combination, and organ and brain regional uptake was assessed at various times after injection by autoradiog. or dissection. Blood and brain samples were assayed for metabolites by high-performance liquid chromatog. CNS-5161 binds brain membranes with high affinity (Kd < 4 nM) and fast association and dissociation kinetics. Specific binding increased in the presence of glutamate and glycine. I.v. administration in control rats resulted in a heterogeneous brain distribution with hippocampus and cortex > thalamus > striatum > cerebellum, and a cortex/cerebellum ratio of 1.4. Pretreatment with NMDA increased the hippocampus-to-cerebellum ratio to 1.6-1.9 while MK801 abolished this increase, resulting in ratios close to 1. Thus, CNS-5161 binds preferentially to the activated state of the NMDA receptor channel in vitro and in vivo. The high affinity and fast kinetics make it compatible with PET imaging of a carbon-11 labeled CNS-5161.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:506940. HCAPLUS Full-text
TITLE: N-Methyl-D-Aspartate Antagonists and Neuropathic Pain: The Search for Relief
AUTHOR(S): Childers, Wayne E., Jr.; Baudy, Reinhardt B.
CORPORATE SOURCE: Department of Chemical Screening Sciences, Wyeth Research, Inc., Princeton, NJ, 08543-8000, USA
SOURCE: Journal of Medicinal Chemistry (2007), 50(11), 2557-2562
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 10 May 2007
AB The role of NMDA inhibitor in neuropathic and pain and it's use in other pain states with cocorrent use of opiates.
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:175521 HCAPLUS Full-text
DOCUMENT NUMBER: 146:229352
TITLE: Substituted benzimidazole compounds as dual nitric oxide synthase inhibitors and μ-opioid

agonists, their preparation, pharmaceutical compositions, and use in therapy

INVENTOR(S): Renton, Paul; Maddaford, Shawn; Rakhit, Suman; Andrews, John

PATENT ASSIGNEE(S): Neuraxon, Inc., Can.

SOURCE: PCT Int. Appl., 139pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007017764	A2	20070215	WO 2006-IB3075	200605 18
WO 2007017764	A3	20070705		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2005-682043P P 200505 18

OTHER SOURCE(S): MARPAT 146:229352

ED Entered STN: 16 Feb 2007

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to benzimidazole compds. of formula I, which express dual nitric oxide synthase (NOS) inhibitory activity and agonist activity at the μ- opioid receptor. In compds. I, R1 is (un)substituted C1-6 alkyl, (un)substituted C1-4 alkyl-aryl, or (un)substituted C1-4 alkyl-heterocyclyl; R2 is selected from H, halo, (un)substituted C1-6 alkyl, (un)substituted C6-10 aryl, (un)substituted C1-4 alkyl-aryl, (un)substituted C2-9 bridged heterocyclyl, (un)substituted C1-4 alkyl-bridged heterocyclyl, (un)substituted C2-9 heterocyclyl, and (un)substituted C1-4 alkyl-heterocyclyl; R3 and R4 are independently selected from H, F, C1-6 alkyl, and C1-6 alkoxy; R5 is H, R7C(=NH)NH(CH2)p, R7NHC(=NH)NH(CH2)p, or R7NHC(=S)NH(CH2)p, where p is 0-2 and R7 is (un)substituted C1-6 alkyl, (un)substituted C6-10 aryl, (un)substituted C1-4 alkyl-aryl, (un)substituted C2-9 heterocyclyl, etc.; and R6 is H, R8C(=NH)NH(CH2)q, R8NHC(=NH)NH(CH2)q, or R8NHC(=S)NH(CH2)q, where q is 0-2 and R8 is nitro, (un)substituted C1-6 alkyl, (un)substituted C6-10 aryl, (un)substituted C1-4 alkyl-aryl, (un)substituted aroyl, etc.; wherein one, but not both, of R5 and R6 are H; including pharmaceutically acceptable salts or

prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I and a pharmaceutically acceptable excipient, as well to the use of the compns. for the treatment or prevention of chronic pain, acute pain, migraine, and neuropathic pain. Substitution of chloro-2,4-dinitrobenzene with N,N-diethylethylenediamine followed by reduction and amidation with 4-ethoxyphenylacetic acid gave amide II, which underwent intramol. heterocyclization, hydrogenation, and coupling with Me thiophene-2-carboximidothioate hydriodide to give benzimidazole III. The compds. of the invention have dual activity as NOS inhibitors and μ-opioid agonists as exemplified by compound III, which expresses IC50 values of 0.44 μM and 4.7 μM towards human neuronal NOS and human endothelial NOS, resp., and IC50 value of 13 nM for binding and EC50 of 0.34 μM for function of μ-opioid receptors.

L21 ANSWER 4 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1204362 HCAPLUS Full-text
DOCUMENT NUMBER: 145:505331
TITLE: Substituted indole compounds having NOS inhibitory activity and their preparation and pharmaceutical composition
INVENTOR(S): Maddaford, Shawn; Ramnauth, Jailall; Rakhit, Suman; Patman, Joanne; Renton, Paul; Annedi, Subhash C.
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 129pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

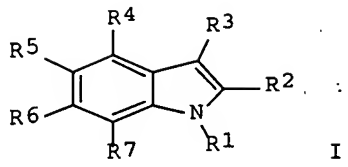
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006258721	A1	20061116	US 2006-404267	200604 13
WO 2007063418	A2	20070607	WO 2006-IB3873	200604 13

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-670856P P 200504 13

OTHER SOURCE(S): MARPAT 145:505331
ED Entered STN: 16 Nov 2006

GI



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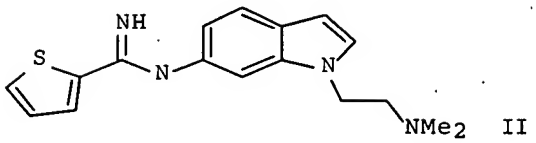

II

AB The invention features compds. of formula I as inhibitors of nitric oxide synthase (NOS), particularly those that selectively inhibit neuronal nitric oxide synthase (nNOS) in preference to other NOS isoforms. The NOS inhibitors of the invention, alone or in combination with other pharmaceutically active agents, can be used for treating or preventing conditions such as, for example, stroke, reperfusion injury, neurodegeneration, head trauma, CABG, migraine headache with and without aura, migraine with allodynia, central post-stroke pain (CPSP), neuropathic pain, morphine/opioid induced tolerance and hyperalgesia. Compds. of formula I wherein R1 is H, (un)substituted C1-6 alkyl, (un)substituted C1-4 alkylaryl, and (un)substituted C1-4 alkylheterocyclyl; R2 and R3 are independently H, halo, (un)substituted C1-6 alkyl, (un)substituted C6-10 aryl, (un)substituted C1-4 alkylaryl, (un)substituted C2-9 bridge heterocyclyl, etc.; R4 and R7 are independently H, F, C1-6 alkyl, and C1-6 alkoxy; R5 is H, R5AC(NH)NH(CH2)r, and R5ANHC(S)NH(CH2)r; r is an integer from 0 to 2; R5A is (un)substituted C1-6 alkyl, (un)substituted C6-10 aryl; (un)substituted C1-4 alkylaryl, etc.; R6 is H, R6AC(NH)(CH2)r and R6ANHC(S)(CH2)r; R6A is equal to R5A; and their pharmaceutically acceptable salts and prodrugs thereof are claimed. Example compound II was prepared by N-alkylation of 6-nitroindole with N,N-dimethyl-2-chloroethylamine; the resulting N-(2-dimethylaminoethyl)-6-nitroindole underwent reduction to give the corresponding 6-aminoindole derivative, which underwent addition to thiophene-2-carboximidothionic acid Ph ester hydrobromide to give compound II. All the invention compds. were evaluated for their NOS inhibitory activity. From the assay, it was determined that compound II exhibited IC50 values of 8.8 μM against Rat nNOS, 109 μM against Murine iNOS, 211 μM against Bovine eNOS, 1.2 μM against Human nNOS, 60 μM against Human iNOS and 15 μM against Human eNOS.

L21 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1059129 HCAPLUS Full-text
DOCUMENT NUMBER: 142:32998
TITLE: Compositions of a cyclooxygenase-2 selective inhibitor and a cannabinoid agent for the treatment of central nervous system damage
INVENTOR(S): Stephenson, Diane T.; Taylor, Duncan P.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 177 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2004105699	A2	20041209	WO 2004-US16496	200405 26
WO 2004105699	A3	20051215		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2006160776	A1	20060720	US 2004-854586	200405 26

PRIORITY APPLN. INFO.: US 2003-473820P P 200305 28

OTHER SOURCE(S): MARPAT 142:32998
ED Entered STN: 10 Dec 2004
AB The present invention provides compns. and methods for the treatment of central nervous system damage in a subject. More particularly, the invention provides a combination therapy for the treatment of a central nervous system ischemic condition or a central nervous system traumatic injury comprising the administration to a subject of a cannabinoid agent in combination with a cyclooxygenase-2 selective inhibitor.

L21 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:645804 HCAPLUS Full-text
DOCUMENT NUMBER: 141:174086
TITLE: Pharmaceutically active compounds containing a guanidine moiety for treatment of neurol. injury and neurodegenerative disorders
INVENTOR(S): Durant, Graham J.; Perlman, Michael; Fischer, James B.; Padmanabhan, Seetharamaiyer
PATENT ASSIGNEE(S): Cambridge Neuroscience, Inc., USA
SOURCE: U.S., 15 pp., Cont.-in-part of U.S. Provisional Ser. No. 63,469.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6774263	B1	20040810	US 1998-169028	199810 09

PRIORITY APPLN. INFO.: US 1997-63469P P 199710 10

ED Entered STN: 11 Aug 2004
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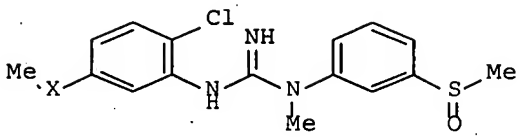

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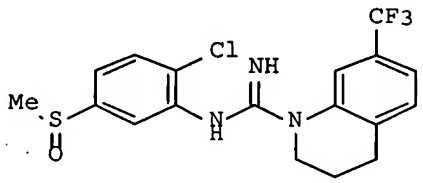


II

AB Compds., such as I (X = S, O) and II, and pharmaceutically acceptable salts thereof, containing a guanidine moiety were prepared for therapeutic use in pharmaceutical compns. for the treatment or prophylaxis of neurol. injury and neurodegenerative disorders. The prepared compds. were assayed for neurol. activity using a rat rotarod motor coordination test.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:353140 HCAPLUS Full-text
DOCUMENT NUMBER: 140:380634
TITLE: Compositions of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for the treatment or prevention of neuropathic pain
INVENTOR(S): Cheung, Raymond Y.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 51 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004082543	A1	20040429	US 2002-282660	20021029
WO 2004039371	A2	20040513	WO 2003-US33089	20031017
WO 2004039371	A3	20040617		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,

KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003277440	A1	20040525	AU 2003-277440	200310 17
PRIORITY APPLN. INFO.:			US 2002-282660	A 200210 29
			WO 2003-US33089	W 200310 17

OTHER SOURCE(S): MARPAT 140:380634
ED Entered STN: 30 Apr 2004
AB The present invention provides compns. and methods to treat or prevent neuropathic pain in a subject using a combination of a COX-2 selective inhibitor and a NMDA receptor antagonist.

L21 ANSWER 8 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:242167 HCAPLUS Full-text
DOCUMENT NUMBER: 138:248536
TITLE: Methods using cholinesterase inhibitors for treating and preventing migraine
INVENTOR(S): Pratt, Raymond
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024456	A1	20030327	WO 2002-US29734	200209 20

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002326977	A1	20030401	AU 2002-326977	200209

PRIORITY APPLN. INFO.:	US 2001-323310P	P	20 200109 20
	US 2002-349244P	P	200201 18
	WO 2002-US29734	W	200209 20

OTHER SOURCE(S): MARPAT 138:248536
ED Entered STN: 28 Mar 2003
AB The invention provides safe and effective methods for treating and preventing migraine by administering an effective amount of one or more cholinesterase inhibitors and, optionally, one or more migraine drugs. The invention also provides compns., combinations, and kits comprising one or more cholinesterase inhibitors and one or more migraine drugs. In one embodiment, the cholinesterase inhibitor is donepezil or ARICEPT.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 9 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:407966 HCAPLUS Full-text
DOCUMENT NUMBER: 138:49371
TITLE: Synthesis and in vitro evaluation of N,N'-diphenyl and N-naphthyl-N'-phenylguanidines as N-methyl-d-aspartate receptor ion-channel ligands
AUTHOR(S): Dumont, Filip; Sultana, Abida; Waterhouse, Rikki N.
CORPORATE SOURCE: Division of Functional Brain Mapping, Columbia University, New York, NY, 10032, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(12), 1583-1586
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:49371
ED Entered STN: 31 May 2002
AB A series of N,N'-diphenyl and N-naphthyl-N'-Ph guanidine derivs. was synthesized as potential N-methyl-D-aspartate (NMDA) receptor positron emission tomog. (PET) ligands. The affinity of the different compds. was determined using in vitro receptor binding assays, and their log P values were estimated using HPLC anal. The effect of N'-3 and N'-3,5 substitution on affinity and lipophilicity was examined The Ki values ranged from 1.87 to 839 nM, while log P values between 1.22 and 2.88 were observed
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:370623 HCAPLUS Full-text
DOCUMENT NUMBER: 137:232425
TITLE: Synthesis of N-(2-chloro-5-methylthiophenyl)-N'-(3-methyl-thiophenyl)-N'-[3H3]methylguanidine,

{[3H3]CNS-5161}
AUTHOR(S): Gibbs, Andrew R.; Morimoto, Hiromi; VanBrocklin, Henry F.; Williams, Philip G.; Biegon, Anat
CORPORATE SOURCE: Department of Functional Imaging, Lawrence Berkeley National Laboratory, Berkeley, CA, 94720, USA
SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals (2002), 45(5), 395-400
CODEN: JLCRD4; ISSN: 0362-4803
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:232425
ED Entered STN: 19 May 2002
AB The preparation of the title compound, [3H3]CNS-5161, was accomplished in three steps starting with the production of [3H3]iodomethane (CT3I). The intermediate N-[3H3]methyl-3-(thiomethylphenyl)cyanamide was prepared in 77% yield by the addition of CT3I to 3- (thiomethylphenyl)cyanamide, previously treated with sodium hydride. Reaction of this tritiated intermediate with 2-chloro-5- thiomethylaniline hydrochloride formed the guanidine compound [3H3]CNS-5161. Purification by HPLC gave the desired labeled product in an overall yield of 9% with >96% radiochem. purity and a final specific activity of 66 Ci mmol-1.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:274772 HCAPLUS Full-text
DOCUMENT NUMBER: 136:363750
TITLE: Early clinical experience with the novel NMDA receptor antagonist CNS 5161
AUTHOR(S): Walters, M. R.; Bradford, A. P. J.; Fischer, J.; Lees, K. R.
CORPORATE SOURCE: Western Infirmary, University Department of Medicine and Therapeutics, Glasgow, G11 6NT, UK
SOURCE: British Journal of Clinical Pharmacology (2002), 53(3), 305-311
CODEN: BCPHBM; ISSN: 0306-5251
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 Apr 2002
AB Aim was to investigate the safety, tolerability and pharmacokinetics of the novel NMDA antagonist CNS 5161 in humans. Excessive activation of glutamate receptors, especially of the N-methyl-D-aspartate (NMDA) subtype has been associated with neuropathic pain, and brain damage caused by focal ischemia in mature brain or hypoxia-ischemia (HI) in neonates. CNS 5161 is a novel NMDA ion-channel antagonist that interacts with the NMDA receptor/ion channel site to produce a noncompetitive blockade of the actions of glutamate. Pre-clin. studies have demonstrated neuroprotective effects of CNS 5161 in the adult rat model of focal cerebral ischemia, as well as anticonvulsant and analgesic effects. This study reports the first administration of CNS 5161 to man. Its objectives were to investigate the hemodynamic effects of the compound, to assess its safety and tolerability in healthy male volunteers, and to provide some preliminary human pharmacokinetic data. We performed a randomized, double-blind placebo controlled phase 1 dose escalation study of CNS 5161. Volunteers were randomized to receive CNS 5161 or placebo in a ratio of 3:1. Twenty-four of 32 healthy volunteers received i.v. infusion of CNS 5161 over 15 min, followed by serial measurements of plasma drug concentration and

hemodynamic observations over 24 h. A dose escalation design was adopted and the volunteers were stratified into eight dosage groups, ranging from 30 μg to 2000 μg. The drug was well tolerated by recipients. Side-effects were dose-related, self limiting and comprised minor subjective sensory symptoms. A dose dependent rise in systolic, mean arterial and diastolic blood pressure was seen in subsequent dosage groups, reaching 23/19 mmHg. Maximal effects were seen between 60 and 120 min after commencement of infusion. All subjects returned to baseline hemodynamic values within 24 h. Putative neuroprotective concns. of CNS 5161 were achieved transiently, although these levels were not sustained. The pharmacokinetic data were best described by a two compartment model. The mean half-life was 2.95 h (s.d. 0.75). Mean clearance was 106 1 h-1 (s.d. 17.8) mean volume of distribution was 296 1 (s.d. 69). These parameters were not significantly affected by body weight This study suggests that CNS 5161 is well tolerated in healthy volunteers within the dose range studied. In addition, information concerning the pharmacokinetics of the compound has been acquired. Studies to investigate the efficacy of the compound in man may now be justified.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:208093 HCAPLUS Full-text
DOCUMENT NUMBER: 134:242673
TITLE: Transdermal administration of n-(2,5-disubstituted phenyl)-n'-(3-substituted phenyl)-n'-methyl guanidines
INVENTOR(S): Van Osdol, William W.; Gale, Robert M.; Brandwein, David H.; Padmanabhan, Rama; Sunram, Joan
PATENT ASSIGNEE(S): Alza Corporation, USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001019352	A1	20010322	WO 2000-US24682	20000908
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2384986	A1	20010322	CA 2000-2384986	20000908
EP 1216036	A1	20020626	EP 2000-964953	20000908
EP 1216036	B1	20051116		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

AT 309791	T	20051215	AT 2000-964953	20000908
ES 2249296	T3	20060401	ES 2000-964953	20000908
US 2003198662	A1	20031023	US 2003-412104	20030411
US 2004258742	A1	20041223	US 2004-895788	20040720
PRIORITY APPLN. INFO.:			US 1999-153996P	P 19990915
			US 2000-658649	B1 20000908
			WO 2000-US24682	W 20000908
			US 2003-412104	B1 20030411

ED Entered STN: 22 Mar 2001

AB A composition for transdermal administration comprises (1) 1-30% a N-(2,5-disubstituted phenyl)-N'-(3-substituted phenyl)-N'-Me guanidine, (2) 0-50% a permeation enhancer, and (3) 30-90% a polymeric carrier. Drug delivery devices and methods for the transdermal administration of a guanidine for the prevention of neuropathic pain, neuropsychol. deficits resulting from cardiac surgery (CABG), and other neurol. disorders are also described. For example, transdermal delivery systems containing 6% guanidine derivative CNS 5161 or its HCl salt CNS 5161A were prepared without or with a permeation enhancer (3% glyceryl monolaurate or 12% lauryl pyroglutamate), and NS 87-2287 acrylate adhesive. Systems with formulations containing the drug as a base displayed higher flux than those with the HCl salt. In addition, systems with formulations containing lauryl pyroglutamate consistently exhibited higher drug flux than formulations with glyceryl monolaurate for formulations with either the drug base or salt.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:177402 HCAPLUS Full-text

DOCUMENT NUMBER: 135:443

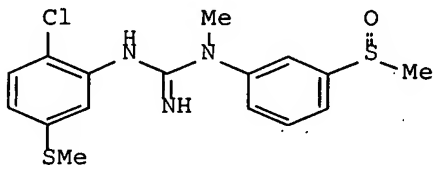
TITLE: Identification and characterization of a potential ischemia-selective N-methyl-d-aspartate (NMDA) receptor ion-channel blocker, CNS 5788

AUTHOR(S): Padmanabhan, S.; Perlman, M. E.; Zhang, L.; Moore, D.; Zhou, D.; Fischer, J. B.; Durant, G. J.; McBurney, R. N.

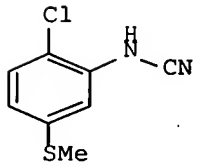
CORPORATE SOURCE: Cambridge NeuroScience, Inc., Norwood, MA,

02602, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(4), 501-504
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 15 Mar 2001
AB The identification and characterization of a potentially ischemia-selective and orally-active sulfoxide based NMDA ion-channel blocker showing good neuroprotective activity, (R)-(+)-N-(2-chloro-5-methylthiophenyl)-N'-(3-methylsulfinylphenyl)- N'-methylguanidine (CNS 5788), is described. Synthesis and in vitro and in vivo studies led to the characterization of a potential ischemia-selective and neuroprotective sulfoxide based ion-channel blocker 10. The R enantiomer has been identified to be orally active and neuroprotective with min. side effects.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:845048 HCAPLUS Full-text
DOCUMENT NUMBER: 134:100623
TITLE: Asymmetric synthesis of a neuroprotective and orally active N-methyl-D-aspartate receptor ion-channel blocker.
AUTHOR(S): Padmanabhan, Seetharamaiyer; Lavin, Ruth C.; Durant, Graham J.
CORPORATE SOURCE: Cambridge NeuroScience, Inc., Cambridge, MA, 02139, USA
SOURCE: Tetrahedron: Asymmetry (2000), 11(17), 3455-3457
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:100623
ED Entered STN: 05 Dec 2000
GI



I



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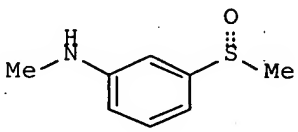


III

AB Asym. synthesis of N-(2-chloro-5-methylthiophenyl)-N'-(3-methylsulfinylphenyl)-N'-methyl-guanidine (I) was achieved in high enantiomeric excess by condensation of cyanamide II and benzeneamine III. The key step involved asym. oxidation of N-methyl-3- methylthioaniline using (1R)-8,8-Dichloro-10- camphorsulfonyloxaziridine (Davis reagent).

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 15 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:545075 HCAPLUS Full-text
DOCUMENT NUMBER: 134:402
TITLE: Neuroprotective, anesthetic, and cardiovascular effects of the NMDA antagonist, CNS 5161A, in isoflurane-anesthetized lambs
AUTHOR(S): Bokesch, Paula M.; Kapural, Miranda; Drummond-Webb, Jonathan; Baird, Kevin; Kapural, Leo; Mee, Roger B. B.; Trapp, Bruce; Starr, Norman J.
CORPORATE SOURCE: Department of Cardiothoracic Anesthesia, Center for Congenital Heart Disease and Surgery, Cleveland, OH, USA
SOURCE: Anesthesiology (2000), 93(1), 202-208
CODEN: ANESAV; ISSN: 0003-3022
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 09 Aug 2000
AB N-methyl-D-aspartate (NMDA) receptor antagonists are neuroprotective in animal models of cerebral ischemia, but adverse cardiovascular and neurobehavioral effects have precluded their clin. use. The authors present the neuroprotective, anesthetic, and cardiovascular effects of a novel NMDA antagonist, CNS 5161A. Lambs, 4.0-6.5 kg, were anesthetized with isoflurane, intubated, and ventilated and had thermodilution catheters placed in the pulmonary artery and 20-g catheters placed in the femoral artery. The min. alveolar concentration (MAC) of isoflurane was determined using the "bracketing technique.". CNS 5161A was given as a bolus and then as an infusion at three doses. Cardiovascular measurements were determined every 15 min. Other lambs (n = 25) were subjected to cardiopulmonary bypass (CPB) with hypothermic circulatory arrest (HCA) for 120 min. Eighteen received CNS 5161A, and seven received saline vehicle. One hour after CPB, brains were perfusion-fixed and removed for in situ hybridization and immunohistochem. anal. in half of the animals. The other half survived 48 h before their brains were examined for neuronal degeneration. Isoflurane at MAC significantly decreased blood pressure, heart rate, cardiac output, and systemic vascular resistance by 30-48% ($n = 16$; $P < 0.05$). CNS 5161A ($n = 12$) had no significant cardiovascular effects. All concns. of CNS 5161A caused a significant reduction (21-29%) of the MAC of isoflurane ($n = 12$; $P < 0.05$). CNS 5161A, at serum concns. greater than 25 ng/mL, completely inhibited c-fos mRNA and c-FOS protein expression in hippocampal neurons after 120 min of HCA, attenuated neuronal degeneration, and improved functional outcome by 47% ($P < 0.05$). CNS 5161A at neuroprotective concns. before CPB-HCA significantly reduces the MAC of isoflurane without cardiovascular effects.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:321805 HCAPLUS Full-text
DOCUMENT NUMBER: 131:80

TITLE: CNS-5161 Cambridge NeuroScience Inc
AUTHOR(S): Linders, Joannes T. M.
CORPORATE SOURCE: Scientific Development Group NV Organon, Oss, 5340 BH, Neth.
SOURCE: Current Opinion in Central & Peripheral Nervous System Investigational Drugs (1999), 1(1), 167-170
CODEN: COCDFA; ISSN: 1464-844X
PUBLISHER: Current Drugs Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 26 May 1999
AB A review with 25 refs. Cambridge NeuroScience is developing CNS-5161, an N-methyl-D-aspartate (NMDA) ion channel blocker, as a potential treatment for neuropathic pain and migraine. It is in phase I development for migraine and neuropathy. Boehringer Ingelheim has the right to negotiate a development and marketing agreement for CNS-5161 for the treatment of neurol. deficits from cardiac surgery [203771], but is not developing the product [231830].
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:265890 HCAPLUS Full-text
DOCUMENT NUMBER: 130:281875
TITLE: Preparation of N-[(methylsulfinyl)phenyl]guanidines as neuroprotectants
INVENTOR(S): Durant, Graham J.; Perlman, Michael; Fischer, James B.; Padmanabhan, Seetharamaiyer
PATENT ASSIGNEE(S): Cambridge Neuroscience, Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9918962	A1	19990422	WO 1998-US21395	19981009
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2306276	A1	19990422	CA 1998-2306276	19981009
AU 9910767	A	19990503	AU 1999-10767	19981009
EP 1041986	A1	20001011	EP 1998-953372	19981009

09

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

JP 2001519393 T 20011023 JP 2000-515597

199810 09

PRIORITY APPLN. INFO.: US 1997-63469P P

199710 10

WO 1998-US21395 W

199810 09

ED Entered STN: 30 Apr 1999

AB Title compds., e.g., MeSZNHC(:NH)NMeC6H4(SOMe)-3.HCl (I) (Z = 2-chloro-1,5-phenylene), were prepared Thus, 3-(MeS)C6H4NHMe was oxidized and the product hydrochloride condensed with 2-chloro-5-methylthiophenylcyanamide to give I.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 18 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:64675 HCAPLUS Full-text

DOCUMENT NUMBER: 130:148681

TITLE: Combination antiinfective drug therapies. comprising aminoglycoside antibiotics and N,N'-disubstituted guanidines

INVENTOR(S): Gwynne, David I.; Durant, Graham J.

PATENT ASSIGNEE(S): Cambridge Neuroscience, Inc., USA

SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902145	A1	19990121	WO 1998-US13640	199807 06

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9882784	A	19990208	AU 1998-82784	199807 06

PRIORITY APPLN. INFO.: US 1997-51860P P

199707 07

WO 1998-US13640 W

199807

OTHER SOURCE(S): MARPAT 130:148681
ED Entered STN: 01 Feb 1999
AB Methods and compns. are provided for treatment of infections, including Gram-neg. and Gram-pos. bacterial infections, comprising administering an aminoglycoside antibiotic in combination with a substituted guanidine or other compound as disclosed. Preferred methods and compns. of the invention will be effective against infections previously treated with aminoglycoside antibiotics, but with decreased occurrence of ototoxicity.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 19 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:119668 HCAPLUS Full-text
DOCUMENT NUMBER: 128:316907
TITLE: Synthesis and Pharmacological Evaluation of N-(2,5-Disubstituted phenyl)-N'-(3-substituted phenyl)-N'-methylguanidines As N-Methyl-D-aspartate Receptor Ion-Channel Blockers. [Erratum to document cited in CA128:212660]
AUTHOR(S): Hu, Lain-Yen; Guo, Junqing; Magar, Sharad S.; Fischer, James B.; Burke-Howie, Kathleen J.; Durant, Graham J.
CORPORATE SOURCE: Cambridge NeuroSci., Inc., Cambridge, MA, 02139, USA
SOURCE: Journal of Medicinal Chemistry (1998), 41(6), 1006
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 28 Feb 1998
AB The generic structure for Table 4 has been corrected

L21 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:94768 HCAPLUS Full-text
DOCUMENT NUMBER: 128:176172
TITLE: Methods of treatment of eye trauma and disorders with substituted guanidines and other compounds
INVENTOR(S): McBurney, Robert N.
PATENT ASSIGNEE(S): Cambridge Neuroscience, Inc., USA; McBurney, Robert N.
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804131	A1	19980205	WO 1997-US13203	199707 25

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,

DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 6242198	B1	20010605	US 1996-686494	199607 25
CA 2261765	A1	19980205	CA 1997-2261765	199707 25
AU 9739654	A	19980220	AU 1997-39654	199707 25
AU 742404	B2	20020103		
EP 918460	A1	19990602	EP 1997-937042	199707 25
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000515895	T	20001128	JP 1998-509048	199707 25
KR 2000029518	A	20000525	KR 1999-700559	199901 23
US 6358696	B1	20020319	US 2000-635309	200008 09
US 2003027801	A1	20030206	US 2002-60101	200201 29
US 6673557	B2	20040106		
PRIORITY APPLN. INFO.:			US 1996-686494 A2	199607 25
			WO 1997-US13203 W	199707 25
			US 2000-635309 A3	200008 09

OTHER SOURCE(S): MARPAT 128:176172
ED Entered STN: 18 Feb 1998
AB Methods using substituted guanidines and other compds. are provided for treatment of eye disorders and injury, including methods for treatment of reduced flow of blood or other nutrients to retinal tissue and/or optic nerve, methods for treatment of retinal ischemia and trauma, and methods for treatment for optic nerve injury/damage.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 21 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:35396 HCAPLUS Full-text

DOCUMENT NUMBER: 128:212660
TITLE: Synthesis and pharmacological evaluation of N-(2,5-disubstituted phenyl)-N'-(3-substituted phenyl)-N'-methylguanidines as N-methyl-D-aspartate receptor ion-channel blockers
AUTHOR(S): Hu, Lain-Yen; Guyo, Junqing; Magar, Sharad S.; Fischer, James B.; Burke-Howie, Kathleen J.; Durant, Graham J.
CORPORATE SOURCE: Cambridge NeuroSci., Inc., Cambridge, MA, 02139, USA
SOURCE: Journal of Medicinal Chemistry (1997), 40(26), 4281-4289
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 22 Jan 1998
AB In the mammalian central nervous system, the N-methyl-D-aspartate (NMDA) subclass of glutamate receptors may play an important role in brain diseases such as stroke, brain or spinal cord trauma, epilepsy, and certain neurodegenerative diseases. Compds. which specifically antagonize the actions of the neurotransmitter glutamate at the NMDA receptor ion-channel site offer a novel approach to treating these disorders. Cerestat (aptiganel, CNS 1102) is currently undergoing clin. trial for the treatment of traumatic brain injury and stroke. Previously, the authors reported that analogs of N-1-naphthyl-N'-(3-ethylphenyl)-N'-methylguanidine bound to the NMDA receptor ion-channel site with high potency and selectivity. Recently, mols. active at both σ receptors and NMDA receptor sites were investigated. A series of substituted diphenylguanidines which are structurally related to N-1-naphthyl-N'-(3-ethylphenyl)-N'-methylguanidine was prepared Compds. containing appropriate substitution pattern in one of the Ph rings of diphenylguanidines displayed high affinity. N-(2,5-dibromophenyl)-N'-(3-ethylphenyl)-N'-methylguanidine (I) had potency at both σ receptors and NMDA receptor sites; I also showed high efficacy in vivo in a neonatal rat excitotoxicity model. Further studies indicated that substituent effects were important in this compound series, and 2,5-disubstituted-Ph was the preferred substitution pattern for high-affinity binding at NMDA receptor sites. N-(2-Bromo-5(methylthio)phenyl)-N'-(3-ethylphenyl)-N'- methylguanidine was highly active at NMDA receptor sites. The binding affinity of some guanidines was further enhanced with the appropriate substitution. Two compds. bound to NMDA receptor sites with high potency and selectivity (Ki vs [3H]MK-801: 1.87 and 1.65 nM, resp.,); these compds. are active in vivo in various animal models of neuroprotection. The structure-activity relationships for these compds. at the NMDA receptor ion-channel site are discussed.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

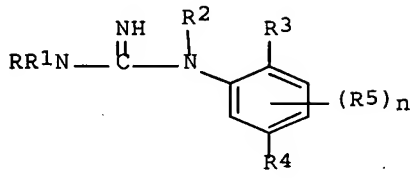
L21 ANSWER 22 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:339509 HCAPLUS Full-text
DOCUMENT NUMBER: 122:96529
TITLE: Substituted guanidines for treatment of central nervous system disease
INVENTOR(S): Durant, Graham J.; Magar, Sharad; Hu, Lain-Yen
PATENT ASSIGNEE(S): Cambridge Neuroscience, Inc., USA
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9427591	A1	19941208	WO 1994-US6008	19940527
W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, TJ, UA, US RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2163361	A1	19941208	CA 1994-2163361	19940527
AU 9470473	A	19941220	AU 1994-70473	19940527
AU 695337	B2	19980813		
ZA 9403744	A	19950426	ZA 1994-3744	19940527
EP 705100	A1	19960410	EP 1994-919275	19940527
EP 705100	B1	20030730		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1126434	A	19960710	CN 1994-192610	19940527
JP 08510754	T	19961112	JP 1995-500988	19940527
JP 3610368	B2	20050112		
AT 245977	T	20030815	AT 1994-919275	19940527
PT 705100	T	20031231	PT 1994-919275	19940527
ES 2204920	T3	20040501	ES 1994-919275	19940527
US 6147063	A	20001114	US 1995-458741	19950602
US 6153604	A	20001128	US 1995-458803	19950602
US 6156741	A	20001205	US 1995-458506	19950602
JP 2004285073	A	20041014	JP 2004-140658	20040511
PRIORITY APPLN. INFO.:			US 1993-68522 A	19930527

US 1993-156773	B2	199311 23
JP 1995-500988	A3	199405 27
WO 1994-US6008	W	199405 27

OTHER SOURCE(S): MARPAT 122:96529
ED Entered STN: 08 Feb 1995
GI



I

AB Treatment of the CNS diseases, which involve excitation of nerve cells by agonists of NMDA receptors, comprises administration of substituted guanidines (I; R = R1 = R2 = H, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, aryl, ets; R3 = R4 = R5 = halogen, OH, azido, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, aryl, etc.; n = 0-3) or their salts. The ED80 and the percentage maximum protection against damage to the CNS for some of the I compds. are presented.

STRUCTURE SEARCH

```
=> file reg
FILE 'REGISTRY' ENTERED AT 17:02:00 ON 02 AUG 2007
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provided by InfoChem.

STRUCTURE FILE UPDATES:     1 AUG 2007  HIGHEST RN 943895-11-2
DICTIONARY FILE UPDATES:    1 AUG 2007  HIGHEST RN 943895-11-2

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  Please note that search-term pricing does apply when
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experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> d stat que l7
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *


Uploading nag204.str
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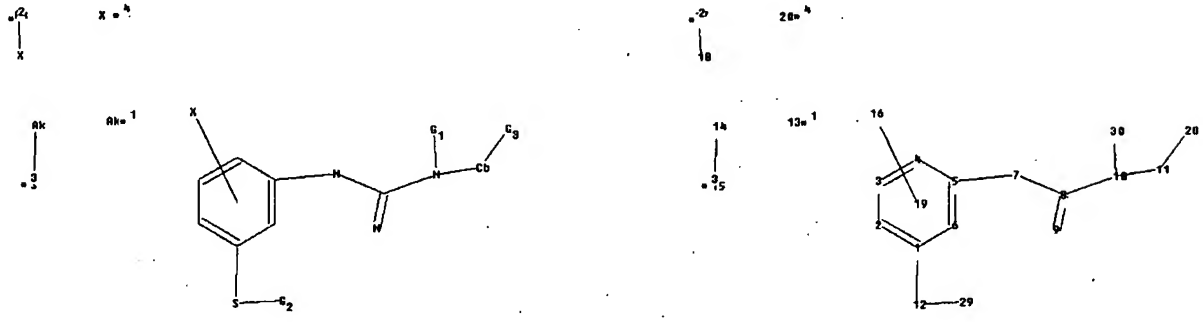

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7  8  9  10  11  12  13  14  15  16  17  18  20  28  29  30
ring nodes :
1  2  3  4  5  6
chain bonds :
1-12  5-7  7-8  8-9  8-10  10-11  10-30  11-28  12-29  14-15  17-18
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6
exact/norm bonds :
1-12  5-7  7-8  8-9  8-10  10-30  11-28  12-29  14-15  17-18
```

```
exact bonds :
10-11
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6


G1:[*1],[*2]

G2:H,[*1]

G3:[*1],[*3],[*4]

Connectivity :
13:1 E exact C  chain  14:1 E exact C  chain
Match level :
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11:CLASS  12:Atom  13:CLASS  14:CLASS  15:Atom  16:CLASS  17:CLASS  18:CLASS
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Generic attributes :
11:
Saturation              : Unsaturated
Type of Ring System     : Monocyclic

Element Count :
Node 11: Limited
    C,C6


Structure attributes must be viewed using STN Express query preparation.
L3            50 SEA FILE=REGISTRY SSS FUL L1
L5               STR


 G1

                D 2
                    T 3


     A 1
 G1 [@1],[@2],[@3]


Structure attributes must be viewed using STN Express query preparation.
L7             7 SEA FILE=REGISTRY SUB=L3 SSS FUL L5

Uploading nag204-1.str
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chain nodes :
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G1:[*1],[*2],[*3]

Match level :
1:Atom 5:Atom 6:Atom 9:Atom

100.0% PROCESSED 50 ITERATIONS 7 ANSWERS
SEARCH TIME: 00.00.01

=> file hcaplus
FILE 'HCAPLUS' ENTERED AT 17:02:15 ON 02 AUG 2007
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FILE COVERS 1907 - 2 Aug 2007 VOL 147 ISS 6
FILE LAST UPDATED: 1 Aug 2007 (20070801/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d que nos l20
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L5              STR
L7            7 SEA FILE=REGISTRY SUB=L3 SSS FUL L5
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L9            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7
L10      133107 SEA FILE=HCAPLUS ABB=ON  PLU=ON  C11/OBI OR 11C/OBI OR
                CARBON/OBI(1A)11/OBI OR 18F/OBI OR F18/OBI OR FLUORINE/OB
                I(1A)18/OBI OR RADIOLABEL?/OBI OR LABEL?/OBI OR ISTOPE/OB
                I OR RADIOPHARMA?/OBI OR RADIO/OBI(W)PHARM?/OBI OR
                IMAG?/OBI (W) (COMPD/OBI OR COMPOUNDS/OBI OR COMPN/OBI)
L11           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 AND L10
L12           4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 OR L11
L16         487 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BRADY, F?/AU
L17         110 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LUTHRA S?/AU
L18          49 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND L17
L19          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L18 AND IMAGING/OBI
L20           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12 NOT L19


=> d ibib ed abs hitstr l20 1-2

L20  ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2006:1356597  HCAPLUS  Full-text
DOCUMENT NUMBER:          146:100417
TITLE:                    Preparation of 18F- or 11C-
                          labeled alkylthiophenyl guanidines as
                          imaging agents
INVENTOR(S):              Robins, Edward George; Arstad, Erik
PATENT ASSIGNEE(S):       Hammersmith Imanet Limited, UK
SOURCE:                   PCT Int. Appl., 35pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
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     WO 2006136846         A1    20061228    WO 2006-GB2315
                                                                    200606
                                                                    23
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA,
             CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
             GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG,
             KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA,
             MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH,
             PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM,
             TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU,
             IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD,
             TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
             ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                    GB 2005-12770       A
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OTHER SOURCE(S): MARPAT 146:100417
ED Entered STN: 29 Dec 2006
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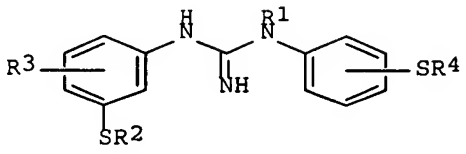

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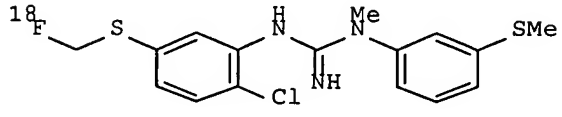
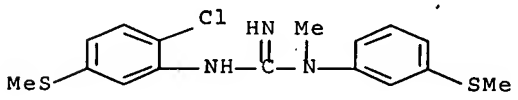


I

AB The invention provides a compound of formula I; or a salt or solvate thereof, wherein: R1 is hydrogen or C1-4alkyl; R2 and R4 are each independently selected from C1-4 alkyl, [11C] C1 4alkyl, and [18F]-C1-4 fluoroalkyl provided that at least one of R2 and R4 is [11C] C1 4alkyl or [18F]-C1-4 fluoroalkyl; and R3 is halo. For example, II was provided in a multi-step synthesis starting from 4-chloro-3-nitrobenzenesulfonyl chloride. Such compds. are useful for imaging central nervous system receptors.

IT **160754-76-7P**, N-(2-Chloro-5-methylthiophenyl)-N'-(3-methylthiophenyl)-N'-methylguanidine **917894-13-4P** **917894-14-5P** **917894-21-4P** **917894-23-6P**, N-(2-Chloro-5-mercaptophenyl)-N'-(3-methylthiophenyl)-N'-methylguanidine **917894-50-9P**
RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of **18F**- or **11C-labeled** alkylthiophenyl guanidines as imaging agents)

RN 160754-76-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (CA INDEX NAME)



RN 917894-13-4 HCAPLUS
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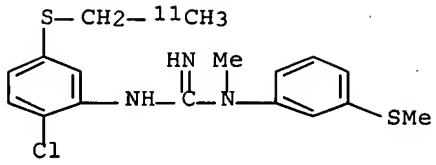
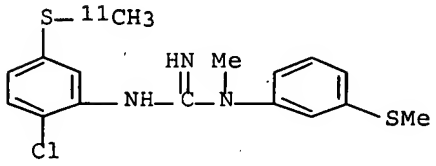


RN 917894-14-5 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methyl-11C-thio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (CA INDEX NAME)



RN 917894-21-4 HCAPLUS
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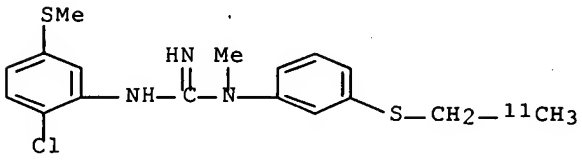

RN 917894-23-6 HCAPLUS
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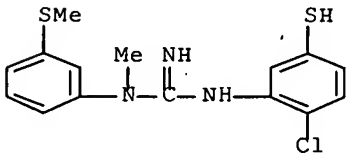

RN 917894-50-9 HCAPLUS
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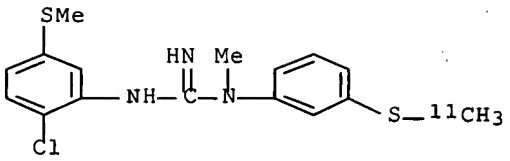
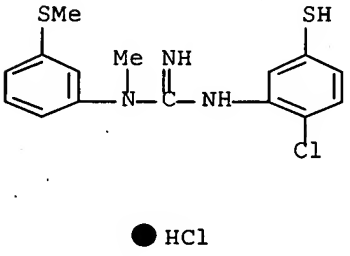


IT **917894-09-8P**, N-(2-Chloro-5-mercaptophenyl)-N'-(3-methylthiophenyl)-N'-methylguanidine hydrochloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of **18F**- or **11C-labeled** alkylthiophenyl guanidines as imaging agents)
RN 917894-09-8 HCAPLUS
CN Guanidine, N'-(2-chloro-5-mercaptophenyl)-N-methyl-N-[3-(methylthio)phenyl]-, hydrochloride (1:1) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:903496 HCAPLUS Full-text
DOCUMENT NUMBER: 138:299872
TITLE: Synthesis of [**11C**] N-(2-chloro-5-thiomethylphenyl)-N'-(3-methoxyphenyl)-N'-methylguanidine ([**11C**]GMOM): a candidate PET tracer for imaging the PCP site of the NMDA ion channel
AUTHOR(S): Waterhouse, Rikki N.; Dumont, Filip; Sultana, Abida; Simpson, Norman; Laruelle, Marc
CORPORATE SOURCE: Department of Psychiatry, Columbia University College of Physicians and Surgeons and New York State Psychiatric Institute, New York, NY, 10032, USA
SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals (2002), 45(11), 955-964
CODEN: JLCRD4; ISSN: 0362-4803
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 29 Nov 2002
AB The N-methyl-D-aspartate (NMDA) ion channel plays an important role in a number of neurodegenerative disorders including stroke, Parkinson's disease, Huntington's Chorea, Alzheimer's disease, schizophrenia and epilepsy. To provide effective radioligands for imaging the PCP binding site of the NMDA

ion channel, we synthesized and characterized in vitro the candidate PCP site ligand N-(2-chloro-5-thiomethylphenyl)-N'-(3-methoxyphenyl)-N'-methylguanidine (GMOM: Ki = 5.2 ± 0.3 nM, log P = 2.34). The corresponding PET radiotracer [11C]GMOM was synthesized with a radiochem. yield of 8.4 ± 3.2% EOS and with a specific activity of 1.23 ± 0.25 Ci/μmol EOS (n = 5). The average time required for synthesis, purification and formulation was 52 ± 5 min. The final product was prepared in a sterile saline solution suitable for in vivo use.

IT **160754-44-9P 160754-76-7P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
([**11C**]GMOM preparation as candidate PET tracer for imaging NMDA ion channel PCP site)

RN 160754-44-9 HCAPLUS
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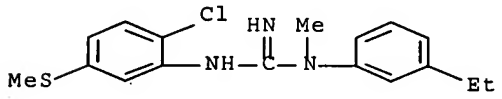
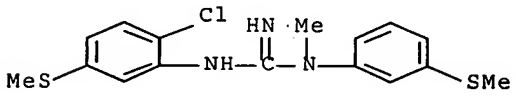


RN 160754-76-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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DICTIONARY FILE UPDATES:   1 AUG 2007  HIGHEST RN 943895-11-2

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REGISTRY includes numerically searchable data for experimental and
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experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html


=> d stat que l3
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
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100.0% PROCESSED    1111 ITERATIONS                          50 ANSWERS
SEARCH TIME: 00.00.01

Uploading nag204.str
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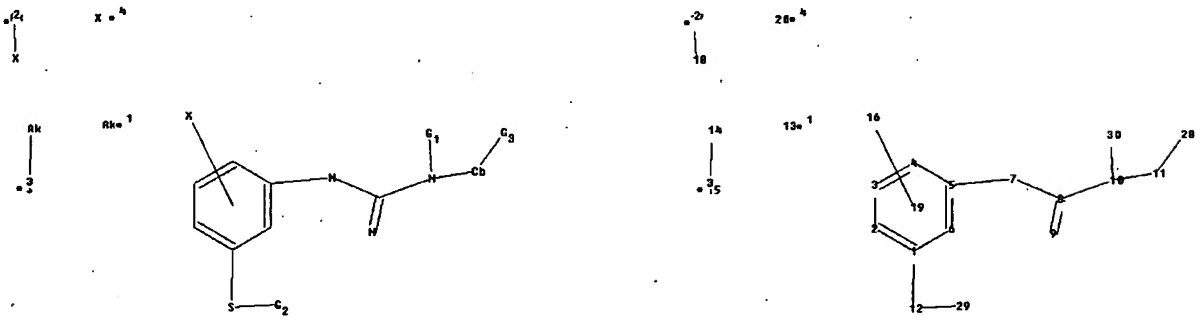

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chain nodes :
7  8  9  10  11  12  13  14  15  16  17  18  20  28  29  30
ring nodes :
1  2  3  4  5  6
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chain bonds :
1-12  5-7  7-8  8-9  8-10  10-11  10-30  11-28  12-29  14-15  17-18
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6
exact/norm bonds :
1-12  5-7  7-8  8-9  8-10  10-30  11-28  12-29  14-15  17-18
exact bonds :
10-11
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6


G1:[*1],[*2]

G2:H,[*1]

G3:[*1],[*3],[*4]

Connectivity :
13:1 E exact C  chain  14:1 E exact C  chain
Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:CLASS  12:Atom  13:CLASS  14:CLASS  15:Atom  16:CLASS  17:CLASS  18:CLASS
19:Atom  20:CLASS  28:CLASS  29:CLASS  30:CLASS
Generic attributes :
11:
Saturation              : Unsaturated
Type of Ring System     : Monocyclic

Element Count :
Node 11: Limited
    C,C6


=> file hcaplus
FILE 'HCAPLUS' ENTERED AT 17:03:00 ON 02 AUG 2007
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FILE COVERS 1907 - 2 Aug 2007  VOL 147 ISS 6
FILE LAST UPDATED: 1 Aug 2007  (20070801/ED)

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 This file contains CAS Registry Numbers for easy and accurate
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L5              STR
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                I OR RADIOPHARMA?/OBI OR RADIO/OBI(W)PHARM?/OBI OR
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L16         487 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BRADY, F?/AU
L17         110 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LUTHRA S?/AU
L18          49 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND L17
L19          13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L18 AND IMAGING/OBI
L21          22 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 NOT (L12 OR L19)

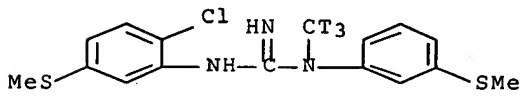

=> d ibib ed abs hitstr l21 1-22

L21  ANSWER 1 OF 22  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:679886  HCAPLUS  Full-text
TITLE:                    In vitro and in vivo characterization of
                          [3H]CNS-5161, a use-dependent ligand for the
                          N-methyl-D-aspartate receptor in rat brain
AUTHOR(S):                Biegon, Anat; Gibbs, Andrew; Alvarado, Maritza;
                          Ono, Michele; Taylor, Scott
CORPORATE SOURCE:         Medical Department, Brookhaven National
                          Laboratory, Upton, NY, USA
SOURCE:                   Synapse (Hoboken, NJ, United States) (2007),
                          61(8), 577-586
                          CODEN: SYNAET; ISSN: 0887-4476
PUBLISHER:                Wiley-Liss, Inc.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
ED   Entered STN:  24 Jun 2007
AB   Glutamate is the major excitatory neurotransmitter in the brain. Glutamate
     activation of the N-methyl-D-aspartate (NMDA) receptor subtype is thought to
     mediate important physiol. and pathol. processes, including memory formation
     and excitotoxicity.  The goal of the present work was to characterize and
     validate a candidate agent for noninvasive positron emission tomog. (PET)
     imaging of this receptor.  [3H]-labeled N-[3-3H]-methyl-3-
     (thiomethylphenyl)cyanamide (CNS-5161) was incubated with rat brain
     homogenates at increasing concns., temps., and times to establish the binding
     kinetics and affinity of the ligand in vitro. Nonspecific binding was measured
     with 100 μM MK-801.  The compound was also injected i.v. in rats pretreated
     with saline, NMDA, MK801, or a combination, and organ and brain regional
     uptake was assessed at various times after injection by autoradiog. or
     dissection. Blood and brain samples were assayed for metabolites by high-
     performance liquid chromatog.  CNS-5161 binds brain membranes with high
     affinity (Kd < 4 nM) and fast association and dissociation kinetics.  Specific
     binding increased in the presence of glutamate and glycine.  I.v.
     administration in control rats resulted in a heterogeneous brain distribution
     with hippocampus and cortex > thalamus > striatum > cerebellum, and a
     cortex/cerebellum ratio of 1.4.  Pretreatment with NMDA increased the
     hippocampus-to-cerebellum ratio to 1.6-1.9 while MK801 abolished this
     increase, resulting in ratios close to 1.  Thus, CNS-5161 binds preferentially
```

to the activated state of the NMDA receptor channel in vitro and in vivo. The high affinity and fast kinetics make it compatible with PET imaging of a carbon-11 labeled CNS-5161.

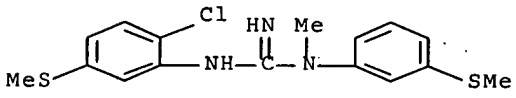
IT **458567-44-7**
RL: ANT (Analyte); BSU (Biological study, unclassified); PKT (Pharmacokinetics); ANST (Analytical study); BIOL (Biological study)
(characterization of [3H]CNS-5161, a use-dependent ligand for NMDA receptor in rat brain and other organs)

RN 458567-44-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-(methyl-t3)-N-[3-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



IT **160754-76-7**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(characterization of [3H]CNS-5161, a use-dependent ligand for NMDA receptor in rat brain and other organs)

RN 160754-76-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (CA INDEX NAME)

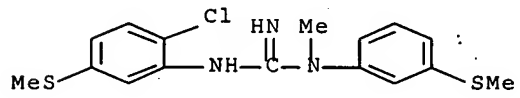


REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:506940 HCAPLUS Full-text
TITLE: N-Methyl-D-Aspartate Antagonists and Neuropathic Pain: The Search for Relief
AUTHOR(S): Childers, Wayne E., Jr.; Baudy, Reinhardt B.
CORPORATE SOURCE: Department of Chemical Screening Sciences, Wyeth Research, Inc., Princeton, NJ, 08543-8000, USA
SOURCE: Journal of Medicinal Chemistry (2007), 50(11), 2557-2562
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 10 May 2007
AB The role of NMDA inhibitor in neuropathic and pain and it's use in other pain states with cocorrent use of opiates.

IT **160754-76-7, CNS 5161**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(N-Methyl-D-Aspartate Antagonists and Neuropathic Pain: The Search for Relief)

RN 160754-76-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:175521 HCAPLUS Full-text
DOCUMENT NUMBER: 146:229352
TITLE: Substituted benzimidazole compounds as dual nitric oxide synthase inhibitors and μ-opioid agonists, their preparation, pharmaceutical compositions, and use in therapy
INVENTOR(S): Renton, Paul; Maddaford, Shawn; Rakhit, Suman; Andrews, John
PATENT ASSIGNEE(S): Neuraxon, Inc., Can.
SOURCE: PCT Int. Appl., 139pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007017764	A2	20070215	WO 2006-IB3075	200605 18
WO 2007017764	A3	20070705		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2005-682043P P 200505 18

OTHER SOURCE(S): MARPAT 146:229352
ED Entered STN: 16 Feb 2007
GI

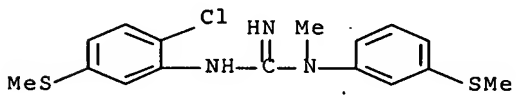
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to benzimidazole compds. of formula I, which express dual nitric oxide synthase (NOS) inhibitory activity and agonist activity at the μ- opioid receptor. In compds. I, R1 is (un)substituted C1-6 alkyl, (un)substituted C1-4 alkyl-aryl, or (un)substituted C1-4 alkyl-heterocyclyl; R2 is selected from H, halo, (un)substituted C1-6 alkyl, (un)substituted C6-10 aryl, (un)substituted C1-4 alkyl-aryl, (un)substituted C2-9 bridged heterocyclyl, (un)substituted C1-4 alkyl-bridged heterocyclyl, (un)substituted C2-9 heterocyclyl, and (un)substituted C1-4 alkyl-heterocyclyl; R3 and R4 are independently selected from H, F, C1-6 alkyl, and C1-6 alkoxy; R5 is H, R7C(=NH)NH(CH2)p, R7NHC(=NH)NH(CH2)p, or R7NHC(=S)NH(CH2)p, where p is 0-2 and R7 is (un)substituted C1-6 alkyl, (un)substituted C6-10 aryl, (un)substituted C1-4 alkyl-aryl, (un)substituted C2-9 heterocyclyl, etc.; and R6 is H, R8C(=NH)NH(CH2)q, R8NHC(=NH)NH(CH2)q, or R8NHC(=S)NH(CH2)q, where q is 0-2 and R8 is nitro, (un)substituted C1-6 alkyl, (un)substituted C6-10 aryl, (un)substituted C1-4 alkyl-aryl, (un)substituted aroyl, etc.; wherein one, but not both, of R5 and R6 are H; including pharmaceutically acceptable salts or prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I and a pharmaceutically acceptable excipient, as well to the use of the compns. for the treatment or prevention of chronic pain, acute pain, migraine, and neuropathic pain. Substitution of chloro-2,4-dinitrobenzene with N,N-diethylethylenediamine followed by reduction and amidation with 4-ethoxyphenylacetic acid gave amide II, which underwent intramol. heterocyclization, hydrogenation, and coupling with Me thiophene-2-carboximidothioate hydriodide to give benzimidazole III. The compds. of the invention have dual activity as NOS inhibitors and μ-opioid agonists as exemplified by compound III, which expresses IC50 values of 0.44 μM and 4.7 μM towards human neuronal NOS and human endothelial NOS, resp., and IC50 value of 13 nM for binding and EC50 of 0.34 μM for function of μ-opioid receptors.

IT **160754-76-7**, N'-[2-Chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]guanidine; **342047-49-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of benzimidazole compds. as dual nitric oxide synthase inhibitors and μ-opioid agonists)

RN 160754-76-7 HCAPLUS

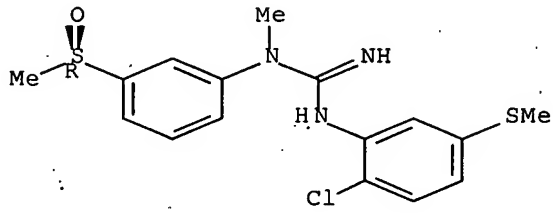
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (CA INDEX NAME)



RN 342047-49-8 HCAPLUS

CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-[(R)-methylsulfinyl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L21 ANSWER 4 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1204362 HCAPLUS Full-text
DOCUMENT NUMBER: 145:505331
TITLE: Substituted indole compounds having NOS inhibitory activity and their preparation and pharmaceutical composition
INVENTOR(S): Maddaford, Shawn; Ramnauth, Jailall; Rakhit, Suman; Patman, Joanne; Renton, Paul; Annedi, Subhash C.
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 129pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006258721	A1	20061116	US 2006-404267	200604 13
WO 2007063418	A2	20070607	WO 2006-IB3873	200604 13

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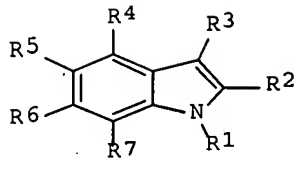
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-670856P P 200504 13

OTHER SOURCE(S): MARPAT 145:505331
ED Entered STN: 16 Nov 2006
GI



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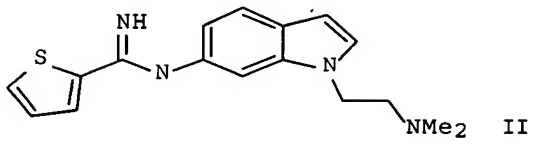


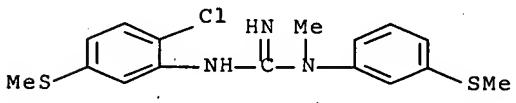
II

AB The invention features compds. of formula I as inhibitors of nitric oxide synthase (NOS), particularly those that selectively inhibit neuronal nitric oxide synthase (nNOS) in preference to other NOS isoforms. The NOS inhibitors of the invention, alone or in combination with other pharmaceutically active agents, can be used for treating or preventing conditions such as, for example, stroke, reperfusion injury, neurodegeneration, head trauma, CABG, migraine headache with and without aura, migraine with allodynia, central post-stroke pain (CPSP), neuropathic pain, morphine/opioid induced tolerance and hyperalgesia. Compds. of formula I wherein R1 is H, (un)substituted C1-6 alkyl, (un)substituted C1-4 alkylaryl, and (un)substituted C1-4 alkylheterocyclyl; R2 and R3 are independently H, halo, (un)substituted C1-6 alkyl, (un)substituted C6-10 aryl, (un)substituted C1-4 alkylaryl, (un)substituted C2-9 bridge heterocyclyl, etc.; R4 and R7 are independently H, F, C1-6 alkyl, and C1-6 alkoxy; R5 is H, R5AC(NH)NH(CH2)r, and R5ANHC(S)NH(CH2)r; r is an integer from 0 to 2; R5A is (un)substituted C1-6 alkyl, (un)substituted C6-10 aryl; (un)substituted C1-4 alkylaryl, etc.; R6 is H, R6AC(NH)(CH2)r and R6ANHC(S)(CH2)r; R6A is equal to R5A; and their pharmaceutically acceptable salts and prodrugs thereof are claimed. Example compound II was prepared by N-alkylation of 6-nitroindole with N,N-dimethyl-2-chloroethylamine; the resulting N-(2-dimethylaminoethyl)-6-nitroindole underwent reduction to give the corresponding 6-aminoindole derivative, which underwent addition to thiophene-2-carboximidothionic acid Ph ester hydrobromide to give compound II. All the invention compds. were evaluated for their NOS inhibitory activity. From the assay, it was determined that compound II exhibited IC50 values of 8.8 μM against Rat nNOS, 109 μM against Murine iNOS, 211 μM against Bovine eNOS, 1.2 μM against Human nNOS, 60 μM against Human iNOS and 15 μM against Human eNOS.

IT **160754-76-7**, N'-[2-Chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]-guanidine **342047-49-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of substituted indole compds. with NOS inhibitory activity useful as therapeutic agents)

RN 160754-76-7 HCAPLUS

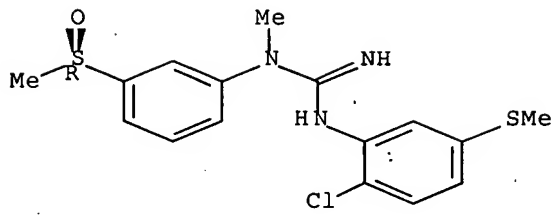
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (CA INDEX NAME)



RN 342047-49-8 HCAPLUS

CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-[(R)-methylsulfinyl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L21 ANSWER 5 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1059129 HCAPLUS Full-text
DOCUMENT NUMBER: 142:32998
TITLE: Compositions of a cyclooxygenase-2 selective inhibitor and a cannabinoid agent for the treatment of central nervous system damage
INVENTOR(S): Stephenson, Diane T.; Taylor, Duncan P.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 177 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004105699	A2	20041209	WO 2004-US16496	200405 26
WO 2004105699	A3	20051215		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006160776	A1	20060720	US 2004-854586	200405 26

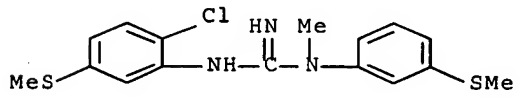
PRIORITY APPLN. INFO.: US 2003-473820P P 200305 28

OTHER SOURCE(S): MARPAT 142:32998
ED Entered STN: 10 Dec 2004
AB The present invention provides compns. and methods for the treatment of central nervous system damage in a subject. More particularly, the invention provides a combination therapy for the treatment of a central nervous system ischemic condition or a central nervous system traumatic injury comprising the

administration to a subject of a cannabinoid agent in combination with a cyclooxygenase-2 selective inhibitor.

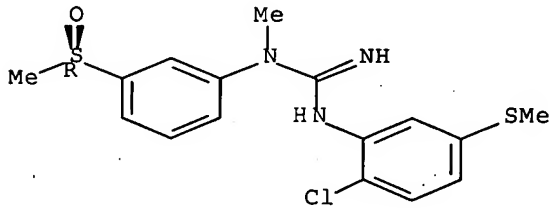
IT **160754-76-7 342047-49-8**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. of a cyclooxygenase-2 selective inhibitor and a cannabinoid agent for treatment of central nervous system damage)

RN 160754-76-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (CA INDEX NAME)



RN 342047-49-8 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-[(R)-methylsulfinyl]phenyl]- (CA INDEX NAME)

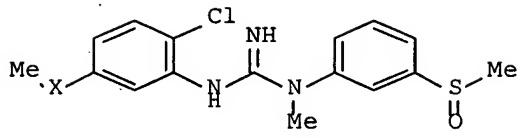
Absolute stereochemistry. Rotation (-).



L21 ANSWER 6 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:645804 HCAPLUS Full-text
DOCUMENT NUMBER: 141:174086
TITLE: Pharmaceutically active compounds containing a guanidine moiety for treatment of neurol. injury and neurodegenerative disorders
INVENTOR(S): Durant, Graham J.; Perlman, Michael; Fischer, James B.; Padmanabhan, Seetharamaiyer
PATENT ASSIGNEE(S): Cambridge Neuroscience, Inc., USA
SOURCE: U.S., 15 pp., Cont.-in-part of U.S. Provisional Ser. No. 63,469.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6774263	B1	20040810	US 1998-169028	19981009
PRIORITY APPLN. INFO.:			US 1997-63469P	P

ED Entered STN: 11 Aug 2004
GI



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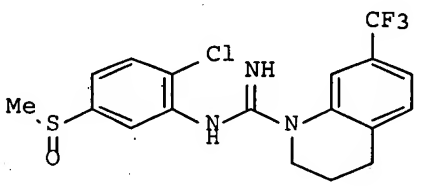


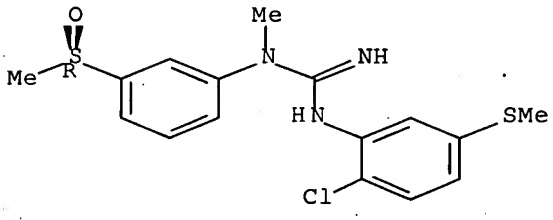
II

AB Compds., such as I (X = S, O) and II, and pharmaceutically acceptable salts thereof, containing a guanidine moiety were prepared for therapeutic use in pharmaceutical compns. for the treatment or prophylaxis of neurol: injury and neurodegenerative disorders. The prepared compds. were assayed for neurol. activity using a rat rotarod motor coordination test.

IT **342047-49-8P 735326-44-0P**
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pharmaceutically active compds. containing a guanidine moiety for treatment of neurol. injury and neurodegenerative disorders)

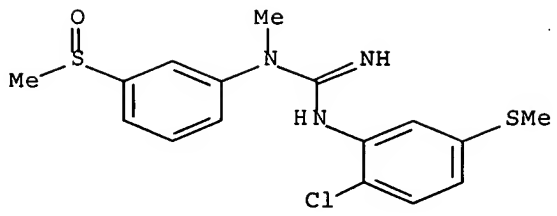
RN 342047-49-8 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-[(R)-methylsulfinyl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



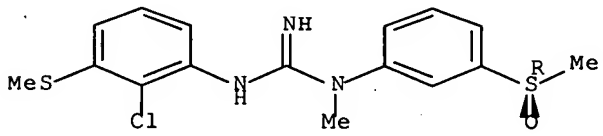
RN 735326-44-0 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylsulfinyl)phenyl]-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).

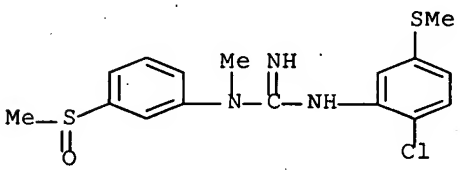


IT **222734-64-7P 222734-69-2P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pharmaceutically active compds. containing a guanidine moiety for treatment of neurol. injury and neurodegenerative disorders)
RN 222734-64-7 HCAPLUS
CN Guanidine, N'-[2-chloro-3-(methylthio)phenyl]-N-methyl-N-[3-[(R)-methylsulfinyl]phenyl]- (9CI) (CA INDEX NAME)

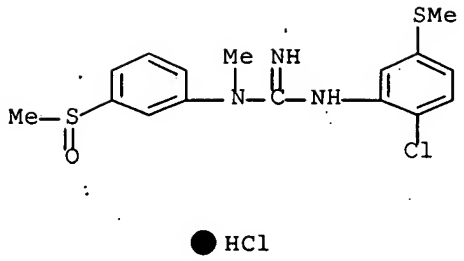
Absolute stereochemistry.



RN 222734-69-2 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylsulfinyl)phenyl]- (9CI) (CA INDEX NAME)



IT **222734-59-0P 222734-65-8P 222734-67-0P**
222734-68-1P 735326-47-3P 735326-48-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pharmaceutically active compds. containing a guanidine moiety for treatment of neurol. injury and neurodegenerative disorders)
RN 222734-59-0 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylsulfinyl)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



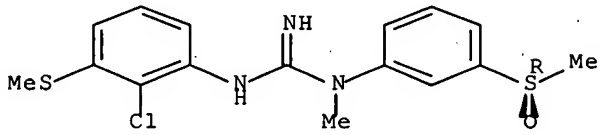
● HCl

RN 222734-65-8 HCAPLUS
CN Guanidine, N'-[2-chloro-3-(methylthio)phenyl]-N-methyl-N-[3-[(R)-methylsulfinyl]phenyl]-, monoacetate (9CI) (CA INDEX NAME)

CM 1

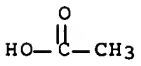
CRN 222734-64-7
CMF C16 H18 Cl N3 O S2 .

Absolute stereochemistry.



CM 2

CRN 64-19-7
CMF C2 H4 O2

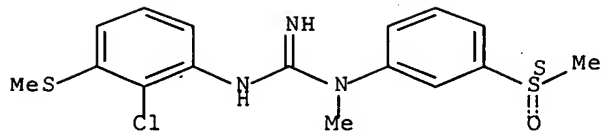


RN 222734-67-0 HCAPLUS
CN Guanidine, N'-[2-chloro-3-(methylthio)phenyl]-N-methyl-N-[3-[(S)-methylsulfinyl]phenyl]-, monoacetate (9CI) (CA INDEX NAME)

CM 1

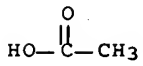
CRN 222734-66-9
CMF C16 H18 Cl N3 O S2

Absolute stereochemistry.



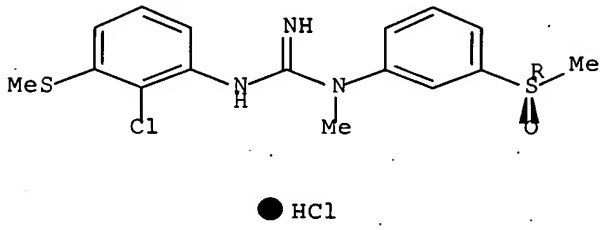
CM 2

CRN 64-19-7
CMF C2 H4 O2



RN 222734-68-1 HCAPLUS
CN Guanidine, N'-[2-chloro-3-(methylthio)phenyl]-N-methyl-N-[3-[(R)-methylsulfinyl]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

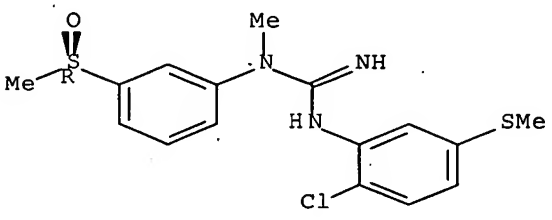


RN 735326-47-3 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-[(R)-methylsulfinyl]phenyl]-, monoacetate (9CI) (CA INDEX NAME)

CM 1

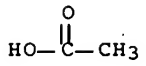
CRN 342047-49-8
CMF C16 H18 Cl N3 O S2

Absolute stereochemistry. Rotation (-).



CM 2

CRN 64-19-7
CMF C2 H4 O2

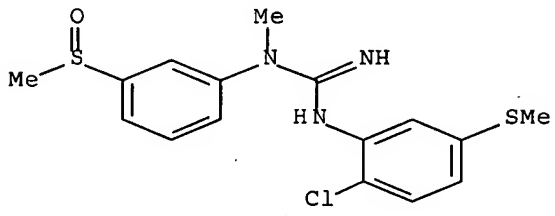


RN 735326-48-4 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylsulfinyl)phenyl]-, (+)-, monoacetate (9CI) (CA INDEX NAME)

CM 1

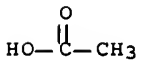
CRN 735326-44-0
CMF C16 H18 Cl N3 O S2

Rotation (+).



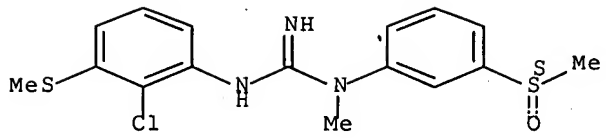
CM 2

CRN 64-19-7
CMF C2 H4 O2



IT **222734-66-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pharmaceutically active compds. containing a guanidine moiety for treatment of neurol. injury and neurodegenerative disorders)
RN 222734-66-9 HCAPLUS
CN Guanidine, N'-[2-chloro-3-(methylthio)phenyl]-N-methyl-N-[3-[(S)-methylsulfinyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



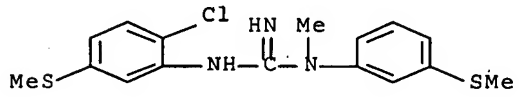
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 7 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:353140 HCAPLUS Full-text
DOCUMENT NUMBER: 140:380634
TITLE: Compositions of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for the treatment or prevention of neuropathic pain
INVENTOR(S): Cheung, Raymond Y.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 51 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004082543	A1	20040429	US 2002-282660	20021029
WO 2004039371	A2	20040513	WO 2003-US33089	20031017
WO 2004039371	A3	20040617		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003277440	A1	20040525	AU 2003-277440	20031017

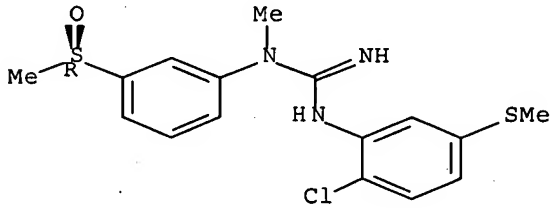
PRIORITY APPLN. INFO.: US 2002-282660 A 20021029
WO 2003-US33089 W 20031017

OTHER SOURCE(S): MARPAT 140:380634
ED Entered STN: 30 Apr 2004
AB The present invention provides compns. and methods to treat or prevent neuropathic pain in a subject using a combination of a COX-2 selective inhibitor and a NMDA receptor antagonist.
IT **160754-76-7 342047-49-8**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (compns. of cyclooxygenase-2 selective inhibitors and NMDA receptor antagonists for treatment or prevention of neuropathic pain)
RN 160754-76-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (CA INDEX NAME)



RN 342047-49-8 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-[(R)-methylsulfinyl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L21 ANSWER 8 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:242167 HCAPLUS Full-text
DOCUMENT NUMBER: 138:248536
TITLE: Methods using cholinesterase inhibitors for treating and preventing migraine
INVENTOR(S): Pratt, Raymond
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

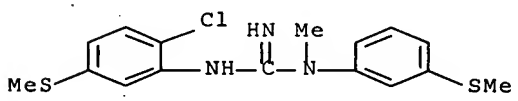
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024456	A1	20030327	WO 2002-US29734	20020920

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002326977	A1	20030401	AU 2002-326977	20020920
PRIORITY APPLN. INFO.:			US 2001-323310P	P 20010920
			US 2002-349244P	P 20020118
			WO 2002-US29734	W 20020920

OTHER SOURCE(S): MARPAT 138:248536
ED Entered STN: 28 Mar 2003
AB The invention provides safe and effective methods for treating and preventing migraine by administering an effective amount of one or more cholinesterase inhibitors and, optionally, one or more migraine drugs. The invention also provides compns., combinations, and kits comprising one or more cholinesterase inhibitors and one or more migraine drugs. In one embodiment, the cholinesterase inhibitor is donepezil or ARICEPT.
IT **160754-76-7**, CNS 5161
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cholinesterase inhibitors for treating and preventing migraine, and use with other agents)
RN 160754-76-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (CA INDEX NAME)



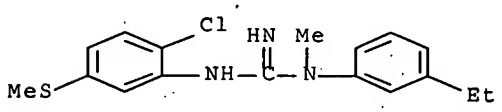
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 9 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:407966 HCAPLUS Full-text
DOCUMENT NUMBER: 138:49371
TITLE: Synthesis and in vitro evaluation of N,N'-diphenyl and N-naphthyl-N'-phenylguanidines as N-methyl-d-aspartate receptor ion-channel ligands

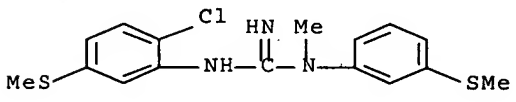
AUTHOR(S): Dumont, Filip; Sultana, Abida; Waterhouse, Rikki N.
CORPORATE SOURCE: Division of Functional Brain Mapping, Columbia University, New York, NY, 10032, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(12), 1583-1586
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:49371
ED Entered STN: 31 May 2002
AB A series of N,N'-diphenyl and N-naphthyl-N'-Ph guanidine derivs. was synthesized as potential N-methyl-D-aspartate (NMDA) receptor positron emission tomog. (PET) ligands. The affinity of the different compds. was determined using in vitro receptor binding assays, and their log P values were estimated using HPLC anal. The effect of N'-3 and N'-3,5 substitution on affinity and lipophilicity was examined The Ki values ranged from 1.87 to 839 nM, while log P values between 1.22 and 2.88 were observed

IT **160754-44-9P 160754-76-7P 160755-23-7P 479500-39-5P 479500-40-8P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and in vitro structure-activity relationship studies of N,N'-di-Ph and N-naphthyl-N'-phenylguanidines as NMDA-receptor ion-channel ligands)

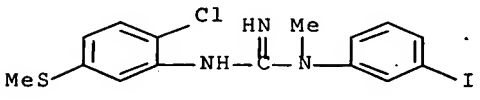
RN 160754-44-9 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-(3-ethylphenyl)-N-methyl- (9CI) (CA INDEX NAME)



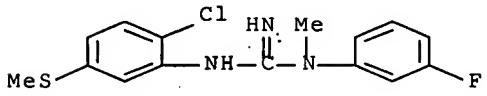
RN 160754-76-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (CA INDEX NAME)



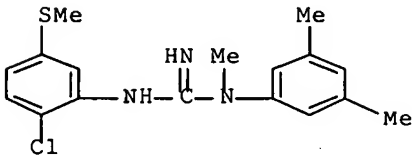
RN 160755-23-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-(3-iodophenyl)-N-methyl- (9CI) (CA INDEX NAME)



RN 479500-39-5 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-(3-fluorophenyl)-N-methyl- (9CI) (CA INDEX NAME)



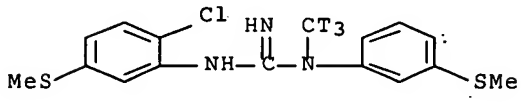
RN 479500-40-8 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-(3,5-dimethylphenyl)-N-methyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 10 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:370623 HCAPLUS Full-text
DOCUMENT NUMBER: 137:232425
TITLE: Synthesis of N-(2-chloro-5-methylthiophenyl)-N'-(3-methyl-thiophenyl)-N'-[3H3]methylguanidine, {[3H3]CNS-5161}
AUTHOR(S): Gibbs, Andrew R.; Morimoto, Hiromi; VanBrocklin, Henry F.; Williams, Philip G.; Biegon, Anat
CORPORATE SOURCE: Department of Functional Imaging, Lawrence Berkeley National Laboratory, Berkeley, CA, 94720, USA
SOURCE: Journal of Labelled Compounds & Radiopharmaceuticals (2002), 45(5), 395-400
CODEN: JLCRD4; ISSN: 0362-4803
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:232425
ED Entered STN: 19 May 2002
AB The preparation of the title compound, [3H3]CNS-5161, was accomplished in three steps starting with the production of [3H3]iodomethane (CT3I). The intermediate N-[3H3]methyl-3-(thiomethylphenyl)cyanamide was prepared in 77% yield by the addition of CT3I to 3- (thiomethylphenyl)cyanamide, previously treated with sodium hydride. Reaction of this tritiated intermediate with 2-chloro-5- thiomethylaniline hydrochloride formed the guanidine compound [3H3]CNS-5161. Purification by HPLC gave the desired labeled product in an overall yield of 9% with >96% radiochem. purity and a final specific activity of 66 Ci mmol-1.
IT **458567-44-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 458567-44-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-(methyl-t3)-N-[3-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

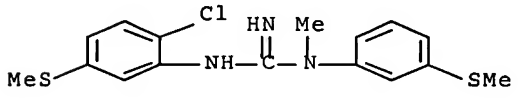
L21 ANSWER 11 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:274772 HCAPLUS Full-text
DOCUMENT NUMBER: 136:363750
TITLE: Early clinical experience with the novel NMDA receptor antagonist CNS 5161
AUTHOR(S): Walters, M. R.; Bradford, A. P. J.; Fischer, J.; Lees, K. R.
CORPORATE SOURCE: Western Infirmary, University Department of Medicine and Therapeutics, Glasgow, G11 6NT, UK
SOURCE: British Journal of Clinical Pharmacology (2002), 53(3), 305-311
CODEN: BCPHBM; ISSN: 0306-5251
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 Apr 2002
AB Aim was to investigate the safety, tolerability and pharmacokinetics of the novel NMDA antagonist CNS 5161 in humans. Excessive activation of glutamate receptors, especially of the N-methyl-D-aspartate (NMDA) subtype has been associated with neuropathic pain, and brain damage caused by focal ischemia in mature brain or hypoxia-ischemia (HI) in neonates. CNS 5161 is a novel NMDA ion-channel antagonist that interacts with the NMDA receptor/ion channel site to produce a noncompetitive blockade of the actions of glutamate. Pre-clin. studies have demonstrated neuroprotective effects of CNS 5161 in the adult rat model of focal cerebral ischemia, as well as anticonvulsant and analgesic effects. This study reports the first administration of CNS 5161 to man. Its objectives were to investigate the hemodynamic effects of the compound, to assess its safety and tolerability in healthy male volunteers, and to provide some preliminary human pharmacokinetic data. We performed a randomized, double-blind placebo controlled phase 1 dose escalation study of CNS 5161. Volunteers were randomized to receive CNS 5161 or placebo in a ratio of 3:1. Twenty-four of 32 healthy volunteers received i.v. infusion of CNS 5161 over 15 min, followed by serial measurements of plasma drug concentration and hemodynamic observations over 24 h. A dose escalation design was adopted and the volunteers were stratified into eight dosage groups, ranging from 30 μg to 2000 μg. The drug was well tolerated by recipients. Side-effects were dose-related, self limiting and comprised minor subjective sensory symptoms. A dose dependent rise in systolic, mean arterial and diastolic blood pressure was seen in subsequent dosage groups, reaching 23/19 mmHg. Maximal effects were seen between 60 and 120 min after commencement of infusion. All subjects returned to baseline hemodynamic values within 24 h. Putative neuroprotective concns. of CNS 5161 were achieved transiently, although these levels were not sustained. The pharmacokinetic data were best described by a two compartment model. The mean half-life was 2.95 h (s.d. 0.75). Mean clearance was 106 1 h-

1 (s.d. 17.8) mean volume of distribution was 296 1 (s.d. 69). These parameters were not significantly affected by body weight This study suggests that CNS 5161 is well tolerated in healthy volunteers within the dose range studied. In addition, information concerning the pharmacokinetics of the compound has been acquired. Studies to investigate the efficacy of the compound in man may now be justified.

IT 160754-76-7, CNS 5161
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel NMDA receptor antagonist CNS 5161 in early clin. experience)

RN 160754-76-7 HCAPLUS

CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 12 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:208093 HCAPLUS Full-text

DOCUMENT NUMBER: 134:242673

TITLE: Transdermal administration of n-(2,5-disubstituted phenyl)-n'-(3-substituted phenyl)-n'-methyl guanidines

INVENTOR(S): Van Osdol, William W.; Gale, Robert M.; Brandwein, David H.; Padmanabhan, Rama; Sunram, Joan

PATENT ASSIGNEE(S): Alza Corporation, USA

SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001019352	A1	20010322	WO 2000-US24682	20000908
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2384986	A1	20010322	CA 2000-2384986	

				20000908
EP 1216036	A1	20020626	EP 2000-964953	20000908
EP 1216036	B1	20051116		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
AT 309791	T	20051215	AT 2000-964953	20000908
ES 2249296	T3	20060401	ES 2000-964953	20000908
US 2003198662	A1	20031023	US 2003-412104	20030411
US 2004258742	A1	20041223	US 2004-895788	20040720
PRIORITY APPLN. INFO.:			US 1999-153996P P	19990915
			US 2000-658649 B1	20000908
			WO 2000-US24682 W	20000908
			US 2003-412104 B1	20030411

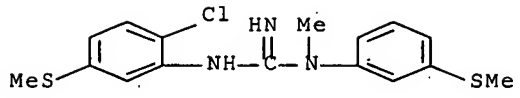
ED Entered STN: 22 Mar 2001

AB A composition for transdermal administration comprises (1) 1-30% a N-(2,5-disubstituted phenyl)-N'-(3-substituted phenyl)-N'-Me guanidine, (2) 0-50% a permeation enhancer, and (3) 30-90% a polymeric carrier. Drug delivery devices and methods for the transdermal administration of a guanidine for the prevention of neuropathic pain, neuropsychol. deficits resulting from cardiac surgery (CABG), and other neurol. disorders are also described. For example, transdermal delivery systems containing 6% guanidine derivative CNS 5161 or its HCl salt CNS 5161A were prepared without or with a permeation enhancer (3% glyceryl monolaurate or 12% lauryl pyroglutamate), and NS 87-2287 acrylate adhesive. Systems with formulations containing the drug as a base displayed higher flux than those with the HCl salt. In addition, systems with formulations containing lauryl pyroglutamate consistently exhibited higher drug flux than formulations with glyceryl monolaurate for formulations with either the drug base or salt.

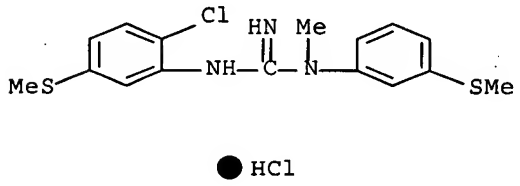
IT **160754-76-7**, CNS 5161 **160756-38-7**, CNS 5161A
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transdermal compns. containing guanidine derivs. for treatment of neurol. disorders)

RN 160754-76-7 HCAPLUS

CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (CA INDEX NAME)



RN 160756-38-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

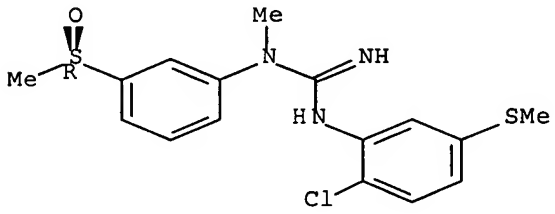
L21 ANSWER 13 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:177402 HCAPLUS Full-text
DOCUMENT NUMBER: 135:443
TITLE: Identification and characterization of a potential ischemia-selective N-methyl-d-aspartate (NMDA) receptor ion-channel blocker, CNS 5788
AUTHOR(S): Padmanabhan, S.; Perlman, M. E.; Zhang, L.; Moore, D.; Zhou, D.; Fischer, J. B.; Durant, G. J.; McBurney, R. N.
CORPORATE SOURCE: Cambridge NeuroScience, Inc., Norwood, MA, 02602, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(4), 501-504
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 15 Mar 2001
AB The identification and characterization of a potentially ischemia-selective and orally-active sulfoxide based NMDA ion-channel blocker showing good neuroprotective activity, (R)-(+)-N-(2-chloro-5-methylthiophenyl)-N'-(3-methylsulfinylphenyl)- N'-methylguanidine (CNS 5788), is described. Synthesis and in vitro and in vivo studies led to the characterization of a potential ischemia-selective and neuroprotective sulfoxide based ion-channel blocker 10. The R enantiomer has been identified to be orally active and neuroprotective with min. side effects.
IT **342047-49-8P**
RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(preparation and characterization of CNS 5788, a ischemia-selective NMDA receptor ion-channel blocker)

RN 342047-49-8 HCAPLUS

CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-[(R)-methylsulfinyl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



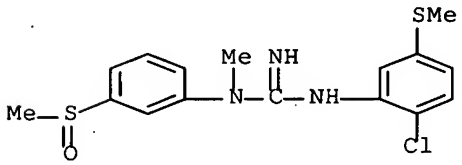
IT **222734-69-2P**

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(preparation and characterization of CNS 5788, a ischemia-selective NMDA receptor ion-channel blocker)

RN 222734-69-2 HCAPLUS

CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylsulfinyl)phenyl]- (9CI) (CA INDEX NAME)



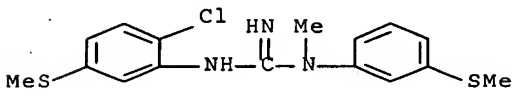
IT **160754-76-7, CNS 5161**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(preparation and characterization of CNS 5788, a ischemia-selective NMDA receptor ion-channel blocker)

RN 160754-76-7 HCAPLUS

CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (CA INDEX NAME)

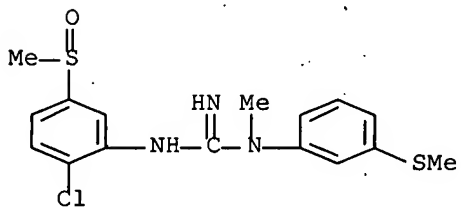


IT **342042-25-5P 342042-26-6P**

RL: BAC (Biological activity or effector, except adverse); BSU

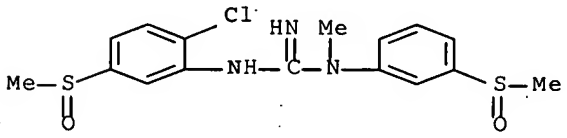
(Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and characterization of CNS 5788, a ischemia-selective NMDA receptor ion-channel blocker)

RN 342042-25-5 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylsulfinyl)phenyl]-N-methyl-N-[3-(methylthio)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



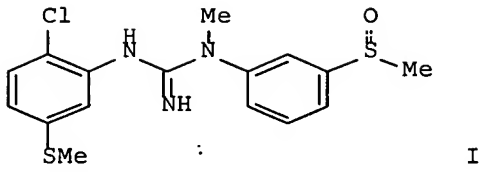
● HCl

RN 342042-26-6 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylsulfinyl)phenyl]-N-methyl-N-[3-(methylsulfinyl)phenyl]- (9CI) (CA INDEX NAME)

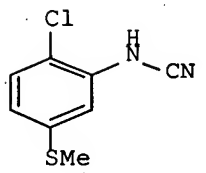


REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

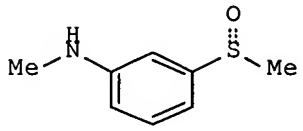
L21 ANSWER 14 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:845048 HCAPLUS Full-text
DOCUMENT NUMBER: 134:100623
TITLE: Asymmetric synthesis of a neuroprotective and orally active N-methyl-D-aspartate receptor ion-channel blocker.
AUTHOR(S): Padmanabhan, Seetharamaiyer; Lavin, Ruth C.; Durant, Graham J.
CORPORATE SOURCE: Cambridge NeuroScience, Inc., Cambridge, MA, 02139, USA
SOURCE: Tetrahedron: Asymmetry (2000), 11(17), 3455-3457
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:100623
ED Entered STN: 05 Dec 2000
GI



I



II



III

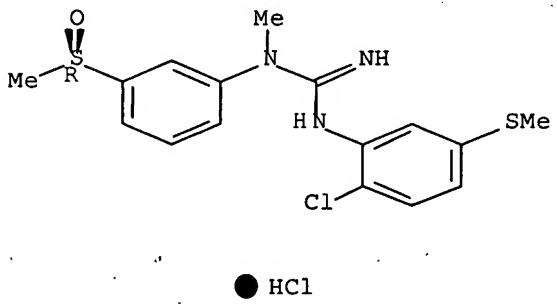
AB Asym. synthesis of N-(2-chloro-5-methylthiophenyl)-N'-(3-methylsulfinylphenyl)-N'-methyl-guanidine (I) was achieved in high enantiomeric excess by condensation of cyanamide II and benzeneamine III. The key step involved asym. oxidation of N-methyl-3- methylthioaniline using (1R)-8,8-Dichloro-10- camphorsulfonyloxaziridine (Davis reagent).

IT **222734-60-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of chiral neuroprotective methylsulfinylguanidine via condensation of methylthiophenylcyanamide and methylsulfinylbenzeneamine prepared by stereoselective oxidation of methylthioaniline with camphorsulfonyloxaziridine)

RN 222734-60-3 HCAPLUS

CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-[(R)-methylsulfinyl]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

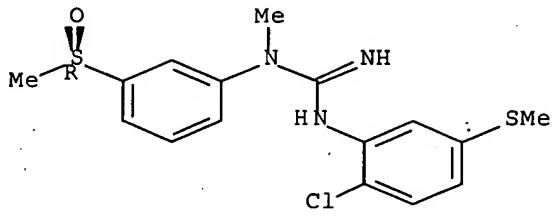


IT **342047-49-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of chiral neuroprotective methylsulfinylguanidine via condensation of methylthiophenylcyanamide and methylsulfinylbenzeneamine prepared by stereoselective oxidation of methylthioaniline with camphorsulfonyloxaziridine)

RN 342047-49-8 HCAPLUS

CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-[(R)-methylsulfinyl]phenyl]- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

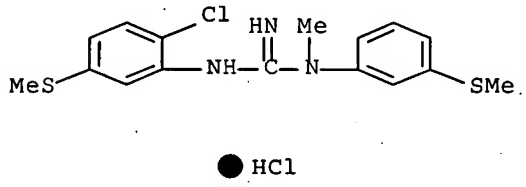
L21 ANSWER 15 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:545075 HCAPLUS Full-text
DOCUMENT NUMBER: 134:402
TITLE: Neuroprotective, anesthetic, and cardiovascular effects of the NMDA antagonist, CNS 5161A, in isoflurane-anesthetized lambs
AUTHOR(S): Bokesch, Paula M.; Kapural, Miranda; Drummond-Webb, Jonathan; Baird, Kevin; Kapural, Leo; Mee, Roger B. B.; Trapp, Bruce; Starr, Norman J.
CORPORATE SOURCE: Department of Cardiothoracic Anesthesia, Center for Congenital Heart Disease and Surgery, Cleveland, OH, USA
SOURCE: Anesthesiology (2000), 93(1), 202-208
CODEN: ANESAV; ISSN: 0003-3022
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 09 Aug 2000
AB N-methyl-D-aspartate (NMDA) receptor antagonists are neuroprotective in animal models of cerebral ischemia, but adverse cardiovascular and neurobehavioral effects have precluded their clin. use. The authors present the neuroprotective, anesthetic, and cardiovascular effects of a novel NMDA antagonist, CNS 5161A. Lambs, 4.0-6.5 kg, were anesthetized with isoflurane, intubated, and ventilated and had thermodilution catheters placed in the pulmonary artery and 20-g catheters placed in the femoral artery. The min. alveolar concentration (MAC) of isoflurane was determined using the "bracketing technique.". CNS 5161A was given as a bolus and then as an infusion at three doses. Cardiovascular measurements were determined every 15 min. Other lambs (n = 25) were subjected to cardiopulmonary bypass (CPB) with hypothermic circulatory arrest (HCA) for 120 min. Eighteen received CNS 5161A, and seven received saline vehicle. One hour after CPB, brains were perfusion-fixed and removed for in situ hybridization and immunohistochem. anal. in half of the animals. The other half survived 48 h before their brains were examined for neuronal degeneration. Isoflurane at MAC significantly decreased blood pressure, heart rate, cardiac output, and systemic vascular resistance by 30-48% (n = 16;P < 0.05). CNS 5161A (n = 12) had no significant cardiovascular effects. All concns. of CNS 5161A caused a significant reduction (21-29%) of the MAC of isoflurane (n = 12;P < 0.05). CNS 5161A, at serum concns. greater than 25 ng/mL, completely inhibited c-fos mRNA and c-FOS protein expression in hippocampal neurons after 120 min of HCA, attenuated neuronal degeneration, and improved functional outcome by 47% (P <

0.05). CNS 5161A at neuroprotective concns. before CPB-HCA significantly reduces the MAC of isoflurane without cardiovascular effects.

IT **160756-38-7**, CNS 5161A
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of NMDA antagonist, CNS 5161A)

RN 160756-38-7 HCAPLUS

CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



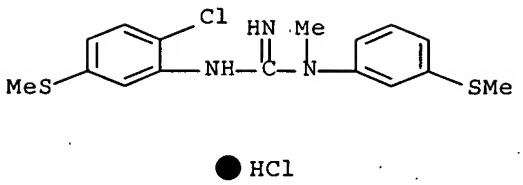
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 16 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:321805 HCAPLUS Full-text
DOCUMENT NUMBER: 131:80
TITLE: CNS-5161 Cambridge NeuroScience Inc
AUTHOR(S): Linders, Joannes T. M.
CORPORATE SOURCE: Scientific Development Group NV Organon, Oss, 5340 BH, Neth.
SOURCE: Current Opinion in Central & Peripheral Nervous System Investigational Drugs (1999), 1(1), 167-170
CODEN: COCDFA; ISSN: 1464-844X
PUBLISHER: Current Drugs Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 26 May 1999
AB A review with 25 refs. Cambridge NeuroScience is developing CNS-5161, an N-methyl-D-aspartate (NMDA) ion channel blocker, as a potential treatment for neuropathic pain and migraine. It is in phase I development for migraine and neuropathy. Boehringer Ingelheim has the right to negotiate a development and marketing agreement for CNS-5161 for the treatment of neurol. deficits from cardiac surgery [203771], but is not developing the product [231830].

IT **160756-38-7**, CNS 5161
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. of CNS-5161)

RN 160756-38-7 HCAPLUS

CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 17 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:265890 HCAPLUS Full-text
DOCUMENT NUMBER: 130:281875
TITLE: Preparation of N-[(methylsulfinyl)phenyl]guanidines as neuroprotectants
INVENTOR(S): Durant, Graham J.; Perlman, Michael; Fischer, James B.; Padmanabhan, Seetharamaiyer
PATENT ASSIGNEE(S): Cambridge Neuroscience, Inc., USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9918962	A1	19990422	WO 1998-US21395	19981009
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2306276	A1	19990422	CA 1998-2306276	19981009
AU 9910767	A	19990503	AU 1999-10767	19981009
EP 1041986	A1	20001011	EP 1998-953372	19981009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001519393	T	20011023	JP 2000-515597	19981009

PRIORITY APPLN. INFO.: US 1997-63469P P 19971017

WO 1998-US21395 W 199810 09

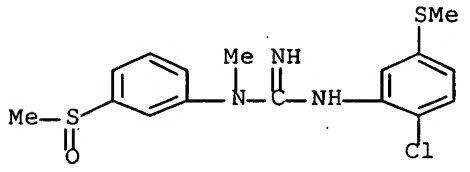
ED Entered STN: 30 Apr 1999

AB Title compds., e.g., MeSZNHC(:NH)NMeC6H4(SOMe)-3.HCl (I) (Z = 2-chloro-1,5-phenylene), were prepared Thus, 3-(MeS)C6H4NHMe was oxidized and the product hydrochloride condensed with 2-chloro-5-methylthiophenylcyanamide to give I.

IT **222734-59-0P 222734-60-3P 222734-61-4P**
222734-64-7P 222734-65-8P 222734-67-0P
222734-68-1P 222734-69-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-[(methylsulfinyl)phenyl]guanidines as neuroprotectants)

RN 222734-59-0 HCAPLUS

CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylsulfinyl)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

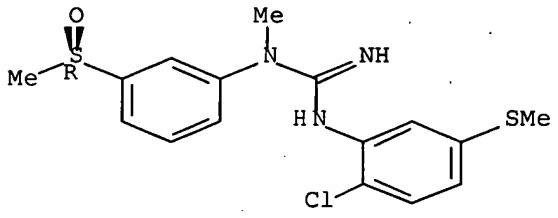


● HCl

RN 222734-60-3 HCAPLUS

CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-[(R)-methylsulfinyl]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

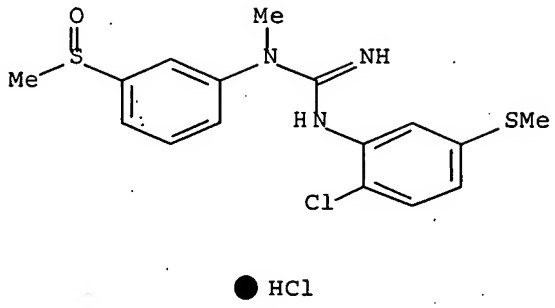


● HCl

RN 222734-61-4 HCAPLUS

CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylsulfinyl)phenyl]-, monohydrochloride, (+)- (9CI) (CA INDEX NAME)

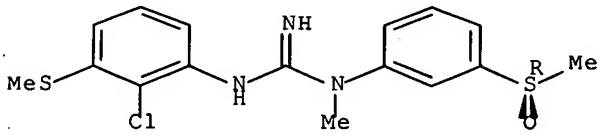
Rotation (+).



● HCl

RN 222734-64-7 HCAPLUS
CN Guanidine, N'-[2-chloro-3-(methylthio)phenyl]-N-methyl-N-[3-[(R)-methylsulfinyl]phenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

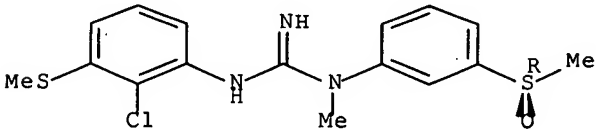


RN 222734-65-8 HCAPLUS
CN Guanidine, N'-[2-chloro-3-(methylthio)phenyl]-N-methyl-N-[3-[(R)-methylsulfinyl]phenyl]-, monoacetate (9CI) (CA INDEX NAME)

CM 1

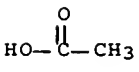
CRN 222734-64-7
CMF C16 H18 Cl N3 O S2

Absolute stereochemistry.



CM 2

CRN 64-19-7
CMF C2 H4 O2

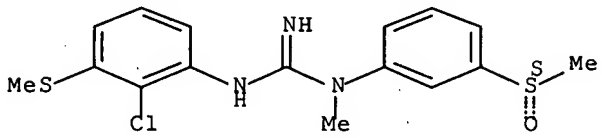


RN 222734-67-0 HCAPLUS
CN Guanidine, N'-[2-chloro-3-(methylthio)phenyl]-N-methyl-N-[3-[(S)-methylsulfinyl]phenyl]-, monoacetate (9CI) (CA INDEX NAME)

CM 1

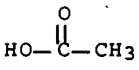
CRN 222734-66-9
CMF C16 H18 Cl N3 O S2

Absolute stereochemistry.



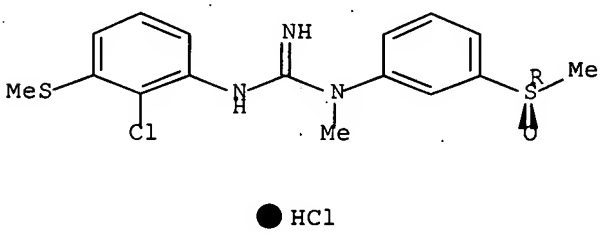
CM 2

CRN 64-19-7
CMF C2 H4 O2

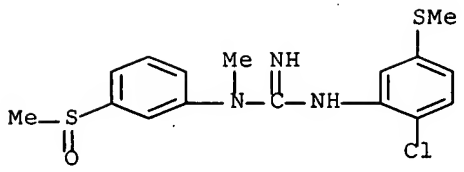


RN 222734-68-1 HCAPLUS
CN Guanidine, N'-[2-chloro-3-(methylthio)phenyl]-N-methyl-N-[3-[(R)-methylsulfinyl]phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 222734-69-2 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylsulfinyl)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 18 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:64675 HCAPLUS Full-text
DOCUMENT NUMBER: 130:148681
TITLE: Combination antiinfective drug therapies comprising aminoglycoside antibiotics and N,N'-disubstituted guanidines
INVENTOR(S): Gwynne, David I.; Durant, Graham J.
PATENT ASSIGNEE(S): Cambridge Neuroscience, Inc., USA
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9902145	A1	19990121	WO 1998-US13640	19980706
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9882784	A	19990208	AU 1998-82784	19980706

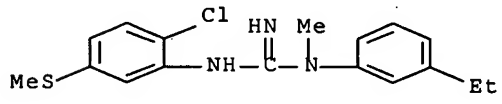
PRIORITY APPLN. INFO.:	US 1997-51860P	P 19970707
	WO 1998-US13640	W 19980706

OTHER SOURCE(S): MARPAT 130:148681
ED Entered STN: 01 Feb 1999
AB Methods and compns. are provided for treatment of infections, including Gram-neg. and Gram-pos. bacterial infections, comprising administering an aminoglycoside antibiotic in combination with a substituted guanidine or other compound as disclosed. Preferred methods and compns. of the invention will be

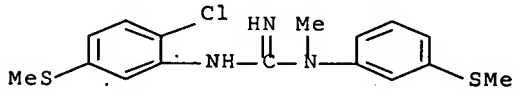
effective against infections previously treated with aminoglycoside antibiotics, but with decreased occurrence of ototoxicity.

IT **160754-44-9 160754-76-7 160755-05-5 160755-08-8 160755-14-6 160755-23-7 160755-30-6 160755-32-8 160755-34-0 160755-36-2 160755-38-4 160755-40-8 160755-42-0 160755-44-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aminoglycoside antibiotic-disubstituted guanidine combination for antiinfective therapy)

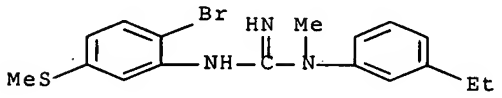
RN 160754-44-9 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-(3-ethylphenyl)-N-methyl- (9CI) (CA INDEX NAME)



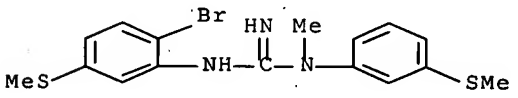
RN 160754-76-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (CA INDEX NAME)



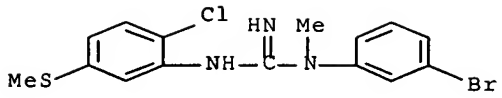
RN 160755-05-5 HCAPLUS
CN Guanidine, N'-[2-bromo-5-(methylthio)phenyl]-N-(3-ethylphenyl)-N-methyl- (9CI) (CA INDEX NAME)



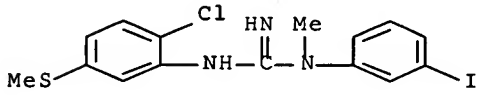
RN 160755-08-8 HCAPLUS
CN Guanidine, N'-[2-bromo-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



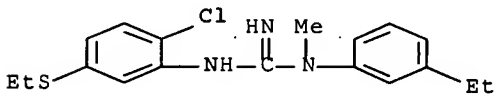
RN 160755-14-6 HCAPLUS
CN Guanidine, N-(3-bromophenyl)-N'-[2-chloro-5-(methylthio)phenyl]-N-methyl- (9CI) (CA INDEX NAME)



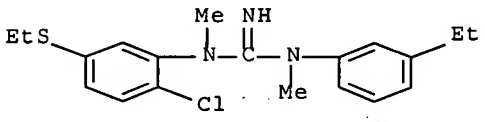
RN 160755-23-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-(3-iodophenyl)-N-methyl- (9CI) (CA INDEX NAME)



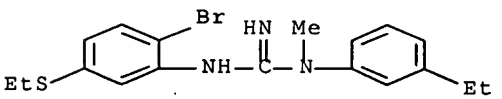
RN 160755-30-6 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(ethylthio)phenyl]-N-(3-ethylphenyl)-N-methyl- (9CI) (CA INDEX NAME)



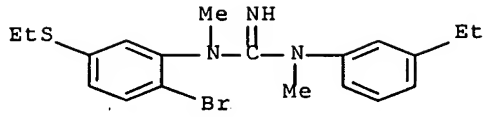
RN 160755-32-8 HCAPLUS
CN Guanidine, N-[2-chloro-5-(ethylthio)phenyl]-N'-(3-ethylphenyl)-N,N'-dimethyl- (9CI) (CA INDEX NAME)



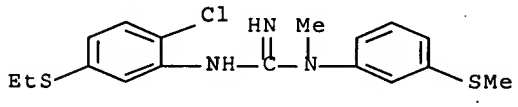
RN 160755-34-0 HCAPLUS
CN Guanidine, N'-[2-bromo-5-(ethylthio)phenyl]-N-(3-ethylphenyl)-N-methyl- (9CI) (CA INDEX NAME)



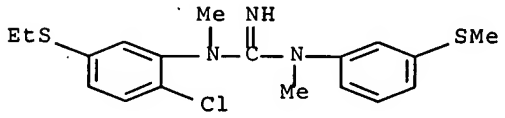
RN 160755-36-2 HCAPLUS
CN Guanidine, N-[2-bromo-5-(ethylthio)phenyl]-N'-(3-ethylphenyl)-N,N'-dimethyl- (9CI) (CA INDEX NAME)



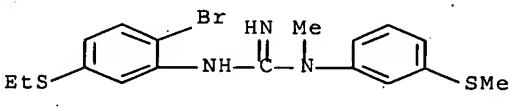
RN 160755-38-4 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(ethylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



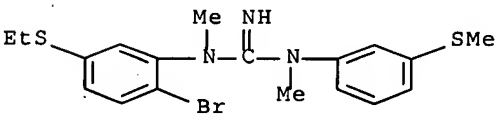
RN 160755-40-8 HCAPLUS
CN Guanidine, N-[2-chloro-5-(ethylthio)phenyl]-N,N'-dimethyl-N'-[3-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



RN 160755-42-0 HCAPLUS
CN Guanidine, N'-[2-bromo-5-(ethylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



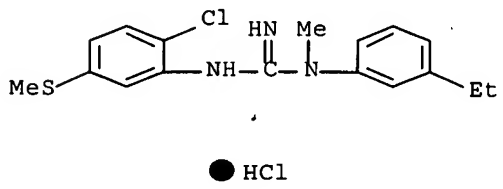
RN 160755-44-2 HCAPLUS
CN Guanidine, N-[2-bromo-5-(ethylthio)phenyl]-N,N'-dimethyl-N'-[3-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



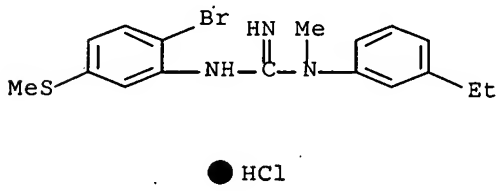
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 19 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:119668 HCAPLUS Full-text

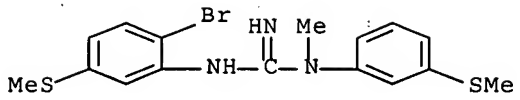
DOCUMENT NUMBER: 128:316907
TITLE: Synthesis and Pharmacological Evaluation of N-(2,5-Disubstituted phenyl)-N'-(3-substituted phenyl)-N'-methylguanidines As N-Methyl-D-aspartate Receptor Ion-Channel Blockers. [Erratum to document cited in CA128:212660]
AUTHOR(S): Hu, Lain-Yen; Guo, Junqing; Magar, Sharad S.; Fischer, James B.; Burke-Howie, Kathleen J.; Durant, Graham J.
CORPORATE SOURCE: Cambridge NeuroSci., Inc., Cambridge, MA, 02139, USA
SOURCE: Journal of Medicinal Chemistry (1998), 41(6), 1006
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 28 Feb 1998
AB The generic structure for Table 4 has been corrected
IT **160756-09-2P 160756-34-3P 160756-39-8P**
204133-09-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and evaluation of substituted phenylmethylguanidines as NMDA receptor blockers (Erratum))
RN 160756-09-2 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-(3-ethylphenyl)-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



RN 160756-34-3 HCAPLUS
CN Guanidine, N'-[2-bromo-5-(methylthio)phenyl]-N-(3-ethylphenyl)-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

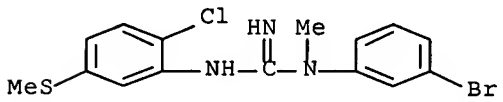


RN 160756-39-8 HCAPLUS
CN Guanidine, N'-[2-bromo-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



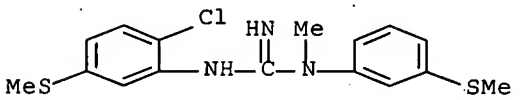
● HCl

RN 204133-09-5 HCAPLUS
CN Guanidine, N-(3-bromophenyl)-N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

IT **160756-38-7P**, CNS 5161
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and evaluation of substituted phenylmethylguanidines as NMDA receptor blockers (Erratum))
RN 160756-38-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

L21 ANSWER 20 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:94768 HCAPLUS Full-text
DOCUMENT NUMBER: 128:176172
TITLE: Methods of treatment of eye trauma and disorders with substituted guanidines and other compounds
INVENTOR(S): McBurney, Robert N.
PATENT ASSIGNEE(S): Cambridge Neuroscience, Inc., USA; McBurney, Robert N.
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804131	A1	19980205	WO 1997-US13203	199707 25
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6242198	B1	20010605	US 1996-686494	199607 25
CA 2261765	A1	19980205	CA 1997-2261765	199707 25
AU 9739654	A	19980220	AU 1997-39654	199707 25
AU 742404	B2	20020103		
EP 918460	A1	19990602	EP 1997-937042	199707 25
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000515895	T	20001128	JP 1998-509048	199707 25
KR 2000029518	A	20000525	KR 1999-700559	199901 23
US 6358696	B1	20020319	US 2000-635309	200008 09
US 2003027801	A1	20030206	US 2002-60101	200201 29
US 6673557	B2	20040106		
PRIORITY APPLN. INFO.:			US 1996-686494 A2	199607 25
			WO 1997-US13203 W	199707 25
			US 2000-635309 A3	200008 09

OTHER SOURCE(S): MARPAT 128:176172
ED Entered STN: 18 Feb 1998
AB Methods using substituted guanidines and other compds. are provided for treatment of eye disorders and injury, including methods for treatment of

reduced flow of blood or other nutrients to retinal tissue and/or optic nerve, methods for treatment of retinal ischemia and trauma, and methods for treatment for optic nerve injury/damage.

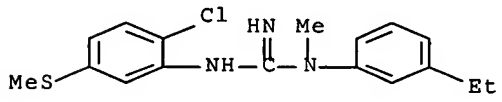
IT **160754-44-9 160754-76-7 160755-05-5 160755-08-8 160755-14-6 160755-23-7 160755-30-6 160755-32-8 160755-34-0 160755-36-2 160755-38-4 160755-40-8 160755-42-0 160755-44-2**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(substituted guanidines and other compds. for treatment of eye trauma and disorders)

RN 160754-44-9 HCAPLUS

CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-(3-ethylphenyl)-N-methyl- (9CI) (CA INDEX NAME)



RN 160754-76-7 HCAPLUS

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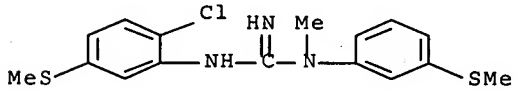
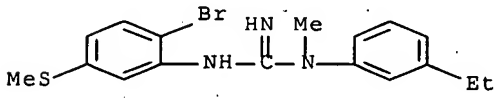


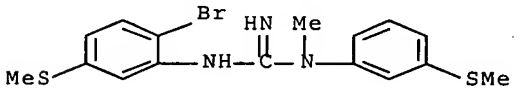
RN 160755-05-5 HCAPLUS

CN Guanidine, N'-[2-bromo-5-(methylthio)phenyl]-N-(3-ethylphenyl)-N-methyl- (9CI) (CA INDEX NAME)



RN 160755-08-8 HCAPLUS

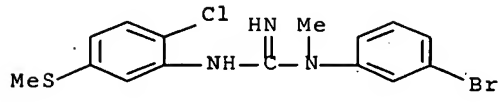
CN Guanidine, N'-[2-bromo-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



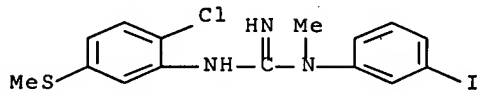
RN 160755-14-6 HCAPLUS

CN Guanidine, N-(3-bromophenyl)-N'-[2-chloro-5-(methylthio)phenyl]-N-

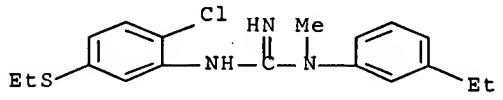
methyl- (9CI) (CA INDEX NAME)



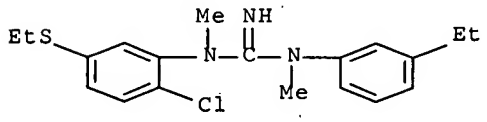
RN 160755-23-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-(3-iodophenyl)-N-methyl- (9CI) (CA INDEX NAME)



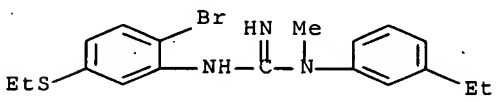
RN 160755-30-6 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(ethylthio)phenyl]-N-(3-ethylphenyl)-N-methyl- (9CI) (CA INDEX NAME)



RN 160755-32-8 HCAPLUS
CN Guanidine, N-[2-chloro-5-(ethylthio)phenyl]-N'-(3-ethylphenyl)-N,N'-dimethyl- (9CI) (CA INDEX NAME)



RN 160755-34-0 HCAPLUS
CN Guanidine, N'-[2-bromo-5-(ethylthio)phenyl]-N-(3-ethylphenyl)-N-methyl- (9CI) (CA INDEX NAME)



RN 160755-36-2 HCAPLUS
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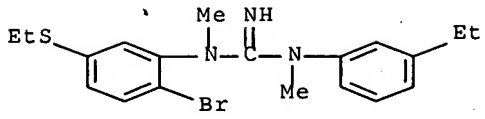

RN 160755-38-4 HCAPLUS
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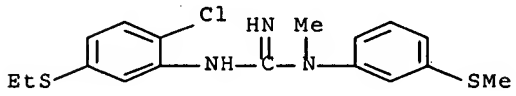

RN 160755-40-8 HCAPLUS
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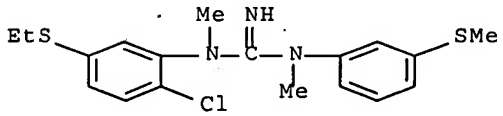
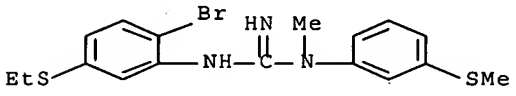
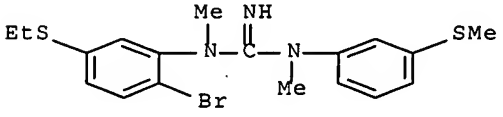


RN 160755-42-0 HCAPLUS
CN Guanidine, N'-[2-bromo-5-(ethylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



RN 160755-44-2 HCAPLUS
CN Guanidine, N-[2-bromo-5-(ethylthio)phenyl]-N,N'-dimethyl-N'-[3-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

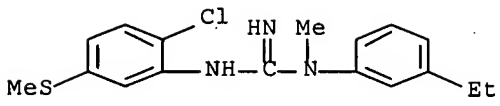
L21 ANSWER 21 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:35396 HCAPLUS Full-text

DOCUMENT NUMBER: 128:212660
TITLE: Synthesis and pharmacological evaluation of N-(2,5-disubstituted phenyl)-N'-(3-substituted phenyl)-N'-methylguanidines as N-methyl-D-aspartate receptor ion-channel blockers
AUTHOR(S): Hu, Lain-Yen; Guyo, Junqing; Magar, Sharad S.; Fischer, James B.; Burke-Howie, Kathleen J.; Durant, Graham J.
CORPORATE SOURCE: Cambridge NeuroSci., Inc., Cambridge, MA, 02139, USA
SOURCE: Journal of Medicinal Chemistry (1997), 40(26), 4281-4289
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 22 Jan 1998

AB In the mammalian central nervous system, the N-methyl-D-aspartate (NMDA) subclass of glutamate receptors may play an important role in brain diseases such as stroke, brain or spinal cord trauma, epilepsy, and certain neurodegenerative diseases. Compds. which specifically antagonize the actions of the neurotransmitter glutamate at the NMDA receptor ion-channel site offer a novel approach to treating these disorders. Cerestat (aptiganel, CNS 1102) is currently undergoing clin. trial for the treatment of traumatic brain injury and stroke. Previously, the authors reported that analogs of N-1-naphthyl-N'-(3-ethylphenyl)-N'-methylguanidine bound to the NMDA receptor ion-channel site with high potency and selectivity. Recently, mols. active at both σ receptors and NMDA receptor sites were investigated. A series of substituted diphenylguanidines which are structurally related to N-1-naphthyl-N'-(3-ethylphenyl)-N'-methylguanidine was prepared Compds. containing appropriate substitution pattern in one of the Ph rings of diphenylguanidines displayed high affinity. N-(2,5-dibromophenyl)-N'-(3-ethylphenyl)-N'-methylguanidine (I) had potency at both σ receptors and NMDA receptor sites; I also showed high efficacy in vivo in a neonatal rat excitotoxicity model. Further studies indicated that substituent effects were important in this compound series, and 2,5-disubstituted-Ph was the preferred substitution pattern for high-affinity binding at NMDA receptor sites. N-(2-Bromo-5(methylthio)phenyl)-N'-(3-ethylphenyl)-N'- methylguanidine was highly active at NMDA receptor sites. The binding affinity of some guanidines was further enhanced with the appropriate substitution. Two compds. bound to NMDA receptor sites with high potency and selectivity (Ki vs [3H]MK-801: 1.87 and 1.65 nM, resp.,); these compds. are active in vivo in various animal models of neuroprotection. The structure-activity relationships for these compds. at the NMDA receptor ion-channel site are discussed.

IT **160756-09-2P 160756-34-3P 160756-39-8P 204133-09-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and evaluation of substituted phenylmethylguanidines as NMDA receptor blockers)

RN 160756-09-2 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-(3-ethylphenyl)-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 160756-34-3 HCAPLUS
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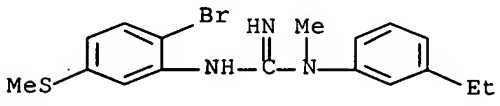
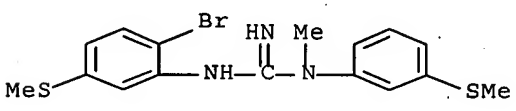


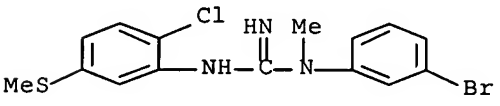
● HCl

RN 160756-39-8 HCAPLUS
CN Guanidine, N'-[2-bromo-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

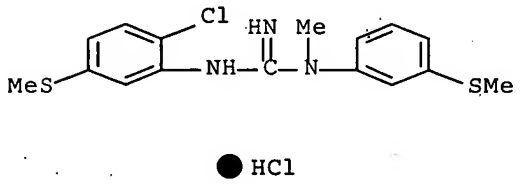
RN 204133-09-5 HCAPLUS
CN Guanidine, N-(3-bromophenyl)-N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

IT **160756-38-7P**, CNS 5161
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and evaluation of substituted phenylmethylguanidines as NMDA receptor blockers)

RN 160756-38-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

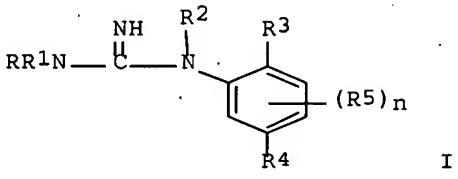
L21 ANSWER 22 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:339509 HCAPLUS Full-text
DOCUMENT NUMBER: 122:96529
TITLE: Substituted guanidines for treatment of central nervous system disease
INVENTOR(S): Durant, Graham J.; Magar, Sharad; Hu, Lain-Yen
PATENT ASSIGNEE(S): Cambridge Neuroscience, Inc., USA
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9427591	A1	19941208	WO 1994-US6008	19940527
W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, TJ, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2163361	A1	19941208	CA 1994-2163361	19940527
AU 9470473	A	19941220	AU 1994-70473	19940527
AU 695337	B2	19980813		
ZA 9403744	A	19950426	ZA 1994-3744	19940527
EP 705100	A1	19960410	EP 1994-919275	19940527
EP 705100	B1	20030730		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1126434	A	19960710	CN 1994-192610	

				199405 27
JP 08510754	T	19961112	JP 1995-500988	199405 27
JP 3610368	B2	20050112		
AT 245977	T	20030815	AT 1994-919275	199405 27
PT 705100	T	20031231	PT 1994-919275	199405 27
ES 2204920	T3	20040501	ES 1994-919275	199405 27
US 6147063	A	20001114	US 1995-458741	199506 02
US 6153604	A	20001128	US 1995-458803	199506 02
US 6156741	A	20001205	US 1995-458506	199506 02
JP 2004285073	A	20041014	JP 2004-140658	200405 11

PRIORITY APPLN. INFO.:	US 1993-68522	A	199305 27
	US 1993-156773	B2	199311 23
	JP 1995-500988	A3	199405 27
	WO 1994-US6008	W	199405 27

OTHER SOURCE(S): MARPAT 122:96529
ED Entered STN: 08 Feb 1995
GI

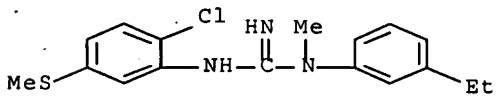


I

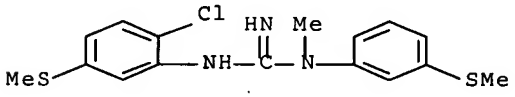
AB Treatment of the CNS diseases, which involve excitation of nerve cells by agonists of NMDA receptors, comprises administration of substituted guanidines (I; R = R1 = R2 = H, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, aryl, ets; R3 = R4 = R5 = halogen, OH, azido, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, aryl, etc.; n = 0-3) or their salts. The ED80 and the percentage maximum protection against damage to the CNS for some of the I compds. are presented.

IT **160754-44-9 160754-76-7 160755-05-5**
160755-08-8 160755-14-6 160755-23-7
160755-30-6 160755-32-8 160755-34-0
160755-36-2 160755-38-4 160755-40-8
160755-42-0 160755-44-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(substituted guanidines for treatment of central nervous system disease)

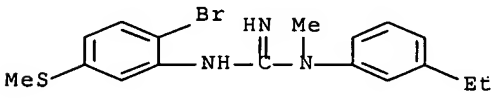
RN 160754-44-9 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-(3-ethylphenyl)-N-methyl- (9CI) (CA INDEX NAME)



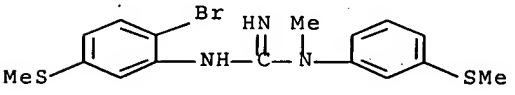
RN 160754-76-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (CA INDEX NAME)



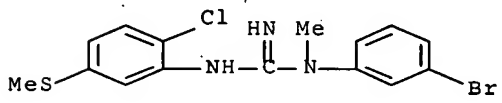
RN 160755-05-5 HCAPLUS
CN Guanidine, N'-[2-bromo-5-(methylthio)phenyl]-N-(3-ethylphenyl)-N-methyl- (9CI) (CA INDEX NAME)



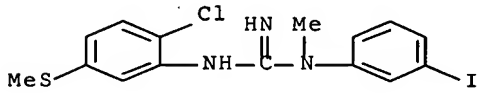
RN 160755-08-8 HCAPLUS
CN Guanidine, N'-[2-bromo-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



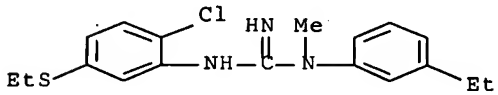
RN 160755-14-6 HCAPLUS
CN Guanidine, N-(3-bromophenyl)-N'-[2-chloro-5-(methylthio)phenyl]-N-methyl- (9CI) (CA INDEX NAME)



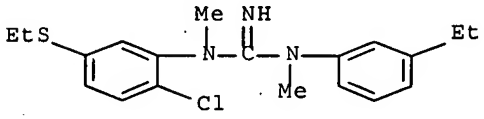
RN 160755-23-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-(3-iodophenyl)-N-methyl- (9CI) (CA INDEX NAME)



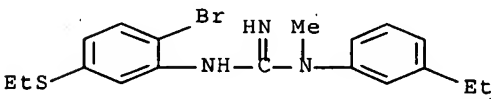
RN 160755-30-6 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(ethylthio)phenyl]-N-(3-ethylphenyl)-N-methyl- (9CI) (CA INDEX NAME)



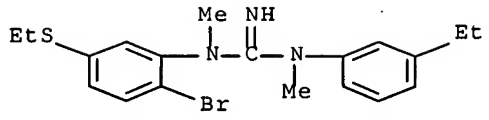
RN 160755-32-8 HCAPLUS
CN Guanidine, N-[2-chloro-5-(ethylthio)phenyl]-N'-(3-ethylphenyl)-N,N'-dimethyl- (9CI) (CA INDEX NAME)



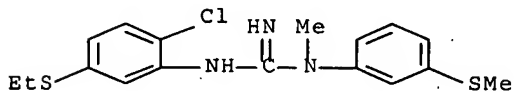
RN 160755-34-0 HCAPLUS
CN Guanidine, N'-[2-bromo-5-(ethylthio)phenyl]-N-(3-ethylphenyl)-N-methyl- (9CI) (CA INDEX NAME)



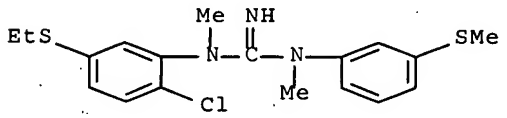
RN 160755-36-2 HCAPLUS
CN Guanidine, N-[2-bromo-5-(ethylthio)phenyl]-N'-(3-ethylphenyl)-N,N'-dimethyl- (9CI) (CA INDEX NAME)



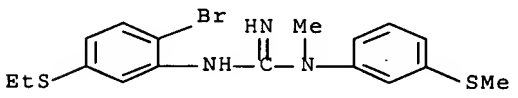
RN 160755-38-4 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(ethylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



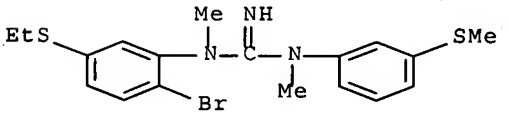
RN 160755-40-8 HCAPLUS
CN Guanidine, N-[2-chloro-5-(ethylthio)phenyl]-N,N'-dimethyl-N'-[3-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



RN 160755-42-0 HCAPLUS
CN Guanidine, N'-[2-bromo-5-(ethylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



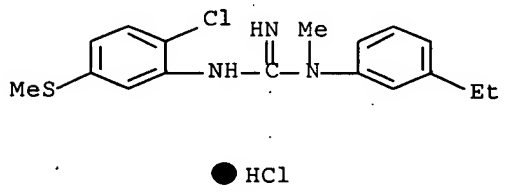
RN 160755-44-2 HCAPLUS
CN Guanidine, N-[2-bromo-5-(ethylthio)phenyl]-N,N'-dimethyl-N'-[3-(methylthio)phenyl]- (9CI) (CA INDEX NAME)



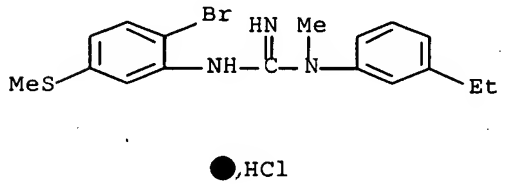
IT **160756-09-2P 160756-34-3P 160756-38-7P**
160756-39-8P 160756-47-8P 160756-52-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL

(Biological study); PREP (Preparation)
(substituted guanidines for treatment of central nervous system disease)

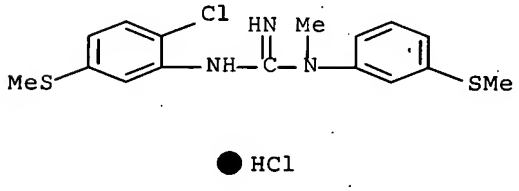
RN 160756-09-2 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-(3-ethylphenyl)-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



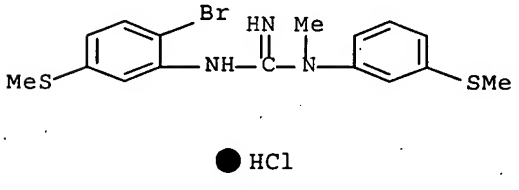
RN 160756-34-3 HCAPLUS
CN Guanidine, N'-[2-bromo-5-(methylthio)phenyl]-N-(3-ethylphenyl)-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



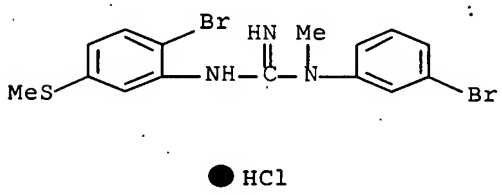
RN 160756-38-7 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)



RN 160756-39-8 HCAPLUS
CN Guanidine, N'-[2-bromo-5-(methylthio)phenyl]-N-methyl-N-[3-(methylthio)phenyl]-, monohydrochloride (9CI) (CA INDEX NAME)

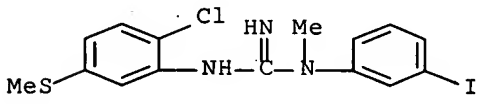


RN 160756-47-8 HCAPLUS
CN Guanidine, N'-[2-bromo-5-(methylthio)phenyl]-N-(3-bromophenyl)-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 160756-52-5 HCAPLUS
CN Guanidine, N'-[2-chloro-5-(methylthio)phenyl]-N-(3-iodophenyl)-N-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

SEARCH HISTORY

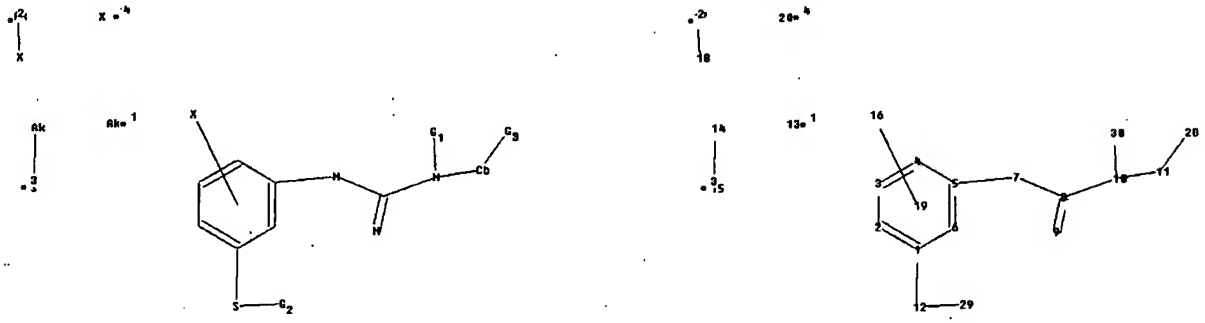
=> d stat que l3
L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L3 50 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 1111 ITERATIONS 50 ANSWERS
SEARCH TIME: 00.00.01

Uploading nag204.str



chain nodes :
7 8 9 10 11 12 13 14 15 16 17 18 20 28 29 30
ring nodes :
1 2 3 4 5 6
chain bonds :
1-12 5-7 7-8 8-9 8-10 10-11 10-30 11-28 12-29 14-15 17-18
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
1-12 5-7 7-8 8-9 8-10 10-30 11-28 12-29 14-15 17-18
exact bonds :
10-11
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

G1:[*1],[*2]

G2:H,[*1]

G3:[*1],[*3],[*4]

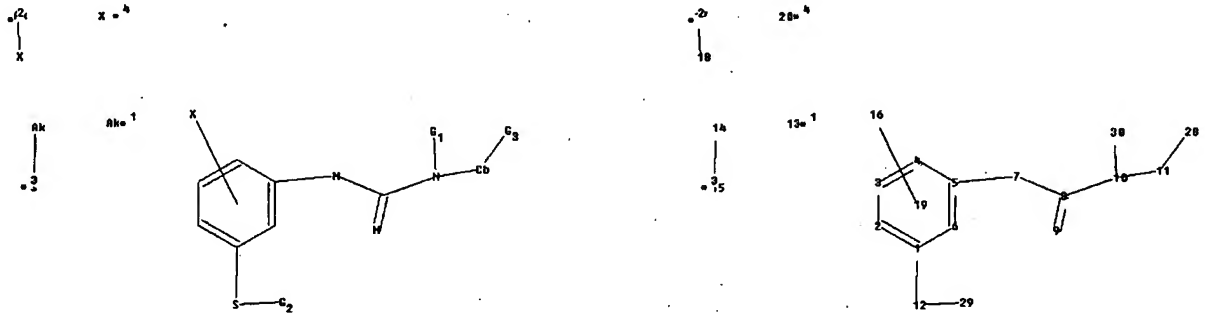
Connectivity :
13:1 E exact C chain 14:1 E exact C chain
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:CLASS 12:Atom 13:CLASS 14:CLASS 15:Atom 16:CLASS 17:CLASS 18:CLASS
19:Atom 20:CLASS 28:CLASS 29:CLASS 30:CLASS
Generic attributes :
11:
Saturation : Unsaturated

```
Type of Ring System     : Monocyclic

Element Count :
Node 11: Limited
    C,C6


=> d stat que l7
L1              STR


Uploading nag204.str
```



```
chain nodes :
7  8  9  10  11  12  13  14  15  16  17  18  20  28  29  30
ring nodes :
1  2  3  4  5  6
chain bonds :
1-12  5-7  7-8  8-9  8-10  10-11  10-30  11-28  12-29  14-15  17-18
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6
exact/norm bonds :
1-12  5-7  7-8  8-9  8-10  10-30  11-28  12-29  14-15  17-18
exact bonds :
10-11
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6


G1:[*1],[*2]

G2:H,[*1]

G3:[*1],[*3],[*4]

Connectivity :
13:1 E exact C  chain  14:1 E exact C  chain
Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:CLASS  12:Atom  13:CLASS  14:CLASS  15:Atom  16:CLASS  17:CLASS  18:CLASS
19:Atom  20:CLASS  28:CLASS  29:CLASS  30:CLASS
Generic attributes :
11:
Saturation              : Unsaturated
Type of Ring System     : Monocyclic
```

```
Element Count :
Node 11: Limited
    C,C6



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
L3           50 SEA FILE=REGISTRY SSS FUL L1
L5              STR


 G1

                D 2
                    T 3


    A 1
G1 [@1],[@2],[@3]


Structure attributes must be viewed using STN Express query preparation.
L7            7 SEA FILE=REGISTRY SUB=L3 SSS FUL L5

100.0% PROCESSED      50 ITERATIONS                          7 ANSWERS
SEARCH TIME: 00.00.01

Uploading nag204-1.str
```

```
chain nodes :
1  5  6  9


G1:[*1],[*2],[*3]

Match level :
1:Atom  5:Atom  6:Atom  9:Atom


=> d his full

     (FILE 'HOME' ENTERED AT 11:16:44 ON 02 AUG 2007)

     FILE 'REGISTRY' ENTERED AT 11:16:52 ON 02 AUG 2007
L1             STRUCTURE UPLOADED
L2           1 SEA SSS SAM L1
L3          50 SEA SSS FUL L1
               SAV NAG204/A L3
L4             STRUCTURE UPLOADED
L5             STRUCTURE UPLOADED
L6           0 SEA SUB=L3 SSS SAM L5
L7           7 SEA SUB=L3 SSS FUL L5
               SAV L7 NAG204A/A

     FILE 'HCAPLUS' ENTERED AT 15:38:08 ON 02 AUG 2007
L8          26 SEA ABB=ON  PLU=ON  L3
L9           3 SEA ABB=ON  PLU=ON  L7
L10     133107 SEA ABB=ON  PLU=ON  C11/OBI OR 11C/OBI OR CARBON/OBI(1A)1
               1/OBI OR 18F/OBI OR F18/OBI OR FLUORINE/OBI(1A)18/OBI OR
               RADIOLABEL?/OBI OR LABEL?/OBI OR ISTOPE/OBI OR RADIOPHARM
               A?/OBI OR RADIO/OBI(W)PHARM?/OBI OR IMAG?/OBI (W)
               (COMPD/OBI OR COMPOUNDS/OBI OR COMPN/OBI)
L11          4 SEA ABB=ON  PLU=ON  L8 AND L10
L12          4 SEA ABB=ON  PLU=ON  L9 OR L11
L16        487 SEA ABB=ON  PLU=ON  BRADY, F?/AU
L17        110 SEA ABB=ON  PLU=ON  LUTHRA S?/AU
L18         49 SEA ABB=ON  PLU=ON  L16 AND L17
L19         13 SEA ABB=ON  PLU=ON  L18 AND IMAGING/OBI
L20          2 SEA ABB=ON  PLU=ON  L12 NOT L19
```

```
L21          22 SEA ABB=ON  PLU=ON  L8 NOT (L12 OR L19)

     FILE 'HCAPLUS' ENTERED AT 17:01:20 ON 02 AUG 2007
               D QUE NOS L21
               D IBIB ED ABS L21 1-22

     FILE 'REGISTRY' ENTERED AT 17:02:00 ON 02 AUG 2007
               D STAT QUE L7

     FILE 'HCAPLUS' ENTERED AT 17:02:15 ON 02 AUG 2007
               D QUE NOS L20
               D IBIB ED ABS HITSTR L20 1-2

     FILE 'REGISTRY' ENTERED AT 17:02:38 ON 02 AUG 2007
               D STAT QUE L3

     FILE 'HCAPLUS' ENTERED AT 17:03:00 ON 02 AUG 2007
               D QUE NOS L21
               D IBIB ED ABS HITSTR L21 1-22
               D STAT QUE L3
               D STAT QUE L7


     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:     1 AUG 2007  HIGHEST RN 943895-11-2
     DICTIONARY FILE UPDATES:    1 AUG 2007  HIGHEST RN 943895-11-2

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     predicted properties as well as tags indicating availability of
     experimental property data in the original document.  For informatio
     on property searching in REGISTRY, refer to:

     http://www.cas.org/support/stngen/stndoc/properties.html

     FILE STNGUIDE
     FILE CONTAINS CURRENT INFORMATION.
     LAST RELOADED: Jul 30, 2007 (20070730/UP).

     FILE HCAPLUS

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